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GYNECOLOGIC TUMORS

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VULVAR TUMORS

1. ULTRASTRUCTURE OF ADENOCARCINOMA OF BARTHOLIN'S GLAND.

Kuzuya K, Matsuyama M, Nishi Y, Chihara T, Suchi T
Dept. Gynecology, Aichi Cancer Center Hosp., Kanokoden, Chikusaku, Nagoya 464, Japan
Cancer; 48(6):1392-1398 1981

The case of a 41-yr-old woman with well-differentiated papillary adenocarcinoma of the Bartholin's gland was studied submicroscopically. The tumor consisted of three types of cells with different types of exocrine secretory granules: (1) Principal cells, which were the most frequently observed component of the tumor, had numerous small, secretory granules of round shape with very high electron density. These granules resembled membrane-bound dense bodies observed in normal Bartholin's duct cells. (2) Goblet-like cells had larger secretory granules with low electron density, resembling secretory granules

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of normal Bartholin's gland cells. (3) Eccrine sweat gland-like cells had large, irregular-shaped secretory granules with moderate electron density. This has been observed in neither normal Bartholin's gland nor duct cells, and resembles secretory granules of eccrine sweat gland cells. Furthermore, fibrillar bodies, frequently described in normal Bartholin's gland cells, were seen in a few tumor cells. These submicroscopic findings suggest that this tumor derived from Bartholin's duct cell, differentiating to gland cell and/or eccrine sweat gland cell. (Author abstract) (12 Refs)

2. HERPESVIRUS-INDUCED ANTIGENS IN SQUAMOUS-CELL CARCINOMA IN SITU OF THE VULVA.

Kaufman RH, Dreesman GR, Burek J, Korhonen MO, Matson DO, Melnick JL, Powell KL, Purifoy DJ, Courtney RJ, Adam E
Dept. Obstetrics and Gynecology, Baylor Coll. Medicine, Houston, TX, 77030
N Engl J Med; 305(9):483-488 1981

Tissue and serum specimens from 19 patients (24-79 yr old) with squamous-cell carcinoma (SCC) in situ of the vulva (10 patients), severe dysplasia (1), condyloma acuminatum (4), and controls seen for periodic check-up (4), were evaluated for herpes simplex virus Type 2 (HSV2) DNA-binding proteins. Nine of 10 biopsy specimens from patients with SCC or severe dysplasia reacted strongly when stained with anti-ICPS34/35 (rabbit antiserum to HSV2-infected-cell-specific protein 34/35), and eight also reacted with anti-VP143 (rabbit antiserum to nonstructural HSV2 protein); five also reacted with anti-ICSP11/12 (rabbit antiserum to HSV2-infected-cell-specific protein 11/12). All the positive reactivity observed with anti-ICSP34/35, anti-ICSP11/12 and anti-VP143 was localized in the cytoplasm rather than the nuclei, as has been previously reported in infected cells. Whole-virion structural antigens were not observed, although serological evidence of previous HSV2 infection was found in patients tested for the presence of antibodies. Serum antibodies to HSV2 were noted in nine patients with SCC, including one with mild dysplasia, and two with normal tissue. The parallel rise in the incidences of HSV2 infection and of vulvar SCC in situ and the demonstration of HSV2-specific proteins in this tissue suggest an association of HSV2 infection with this cancer. (17 Refs)

VAGINAL TUMORS

3. MIXED TUMORS OF THE VAGINA. A CLINICOPATHOLOGICAL ANALYSIS OF EIGHT CASES.

Sirota RL, Dickersin GR, Scully RE
Greater Baltimore Medical Center, 6701 North Charles St., Baltimore, MD, 21204
Am J Surg Pathol; 5(5):413-422 1981

The distinctive clinical, gross, and microscopic features of eight mixed tumors of the vagina are described. Patient age ranged between 20 and 53 yr (av 31); two women were nulliparous and parity for the others, when known, was 1-2. Seven of the eight tumors occurred in or near the hymenal ring. All lesions were treated by local excision. Follow-up of 2-9 yr in seven cases revealed no evidence of recurrence or metastasis. Specimens were described as discrete 1.5-5.0 cm masses composed of pale gray or pink uniformly soft tissue. Light microscopical examination of 7/8 tumors revealed well-circumscribed unencapsulated submucosal nodules. All tumors were moderately to markedly cellular, and composed of stromal-type cells and well-differentiated epithelial elements. Electron microscopy made evident areas composed of small oval stromal-type cells and islands of squamous cells, but no spindle-shaped cells or mucinous glands. Histogenesis of these tumors is unclear: the epithelial components of the mixed tumors may have been of mullerian or urogenital sinus origin. Interrelation of the constituent epithelial and stromal-type cells is also unknown. (20 Refs)

CERVICAL AND UTERINE TUMORS

4. CT OF INTRAMURAL ENDOMETRIAL CARCINOMA: CONTRAST ENHANCEMENT IS ESSENTIAL.

Hamlin DJ, Burgener FA, Beecham JB
Dept. Radiology, Univ. Florida Coll. Medicine, Box J-374, JHMHC, Gainesville, FL, 32610
AJR; 137(3):551-554 1981

The accuracy of computed tomography (CT) in recognizing early stage endometrial carcinoma was assessed in a prospective study in 10 patients in whom macroscopic and microscopic findings of the surgical specimen were correlated with the CT findings. In no instance was endometrial carcinoma confined to the uterine wall demonstrated on a precontrast examination. However, after iv infusion of 300 ml diatrizoate 30%, all seven carcinomas involving one-third or more of the thickness of the uterine wall were clearly demonstrated as hypodense lesions. In three patients the center of the hypodense lesion was significantly more enhanced and this was found at surgery to represent less necrotic tumor. Three carcinomas with lesser intramural extent were still invisible after contrast infusion. Because of slow contrast material accumulation in the myometrium and a delayed washout, the optimum time for scanning appears to be immediately after termination of the infusion when the bladder is not yet densely opaque since this may cause disturbing artifacts. The depth of myometrial invasion by endometrial carcinoma is an important prognostic factor in the disease and the CT demonstration of tumor extent may prove to be valuable in optimizing the selection of surgical and/or radiotherapeutic procedures. (Author abstract) (16 Refs)

5. ULTRASONOGRAPHY IN THE STAGING OF ENDOMETRIAL ADENOCARCINOMA.

Requard CK, Wicks JD, Mettler FA
Dept. Radiology, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131
Radiology; 140(3):781-785 1981

Adenocarcinoma of the endometrium commonly presents at an early stage and is rea dily diagnosed by dilatation and curettage. Ultrasound has not been accurate in differentiating this malignant neoplasm from benign causes of uterine enlargement such as leiomyoma. In this study, the sonographic findings in 21 patients with adenocarcinoma of the endometrium were compared with the clinical and pathological findings. Although no ultrasound criteria were diagnostic of carcinoma, there were statistically significant differences in uterine shape and echo pattern between Stage I-II and Stage III-IV disease: 94% of patients with Stage I-II disease had a normal or bulbous uterus and a normal or hypoechoic parenchymal pattern, while patients with a lobular uterus and/or mixed echo pattern had Stage III-IV. The only clinical errors in staging were in cases of Stage II or III disease. Ultrasound may be helpful in pre-

treatment staging of more difficult cases. (Author abstract) (15 Refs)

6. A CLINICOPATHOLOGICAL STUDY ON MICROINVASIVE CARCINOMA (STAGE IA) OF THE UTERINE CERVIX.

Yoshida S
Dept. Obstetrics and Gynecology, Nagasaki Univ., Sch. Medicine, Sakamoto-cho, Nagasaki 852, Japan
Nippon Sanka Fujinka Gakkai Zasshi; 33(1):127-135 1981

A pathological study of 142 cases of Stage I carcinoma of the uterine cervix with a depth of invasion of less than 5 mm showed 119 of them, 104 Stage Ia (87.4%) and 15 Stage Ib (12.6%), to have a depth of invasion of less than 3 mm. As to the histological pattern of invasion in Stage Ia, advanced bulky outgrowth from glands and early stromal invasion were observed at nearly the same frequency. Of 15 cases of Stage Ib cervical carcinoma with depth of invasion of less than 3 mm, 10 were of reticular invasion, 4 were of fruhe Stroma-arrosin and one was of vessel permeation. With either pattern of invasion, annular and longitudinal extension of the lesion tended to be wider in Stage Ib than in Stage Ia. Spread to the ectocervix was also wider in Stage Ib. Modalities of treatment used for stage Ia carcinoma of the cervix were extended radical hysterectomy in 28 cases, sub-extended hysterectomy in 68 cases, simple hysterectomy in three cases, conizatcn in one case and radiotherapy in four cases. Lymph node metastasis was noted in none of Stage I cervical cancer cases with a depth of invasion of less than 5 mm. (Author abstract) (35 Refs) (In JPN)

7. EPITHELIAL CHANGES IN THE CERVIX: CYTOLOGICAL AND HISTOLOGICAL CORRELATION.

Slavin G, Hudson E
Section Histopathology, Clinical Res. Center, Watford Road, Harrow, Middlesex HA1 3UJ, England
Clin Obstet Gynaecol; 8(1):51-64 1981

Precancerous lesions in the cervical epithelium are reviewed with special emphasis on the role of cytological and histological examination for the differential diagnosis between the potentially malignant (dysplasia and carcinoma in situ) and benign (reactive and inflammatory changes) lesions. The p resence of abnormal dyskaryotic cells in the cervical smears can indicate the need for cervical biopsy. The dyskaryotic cells usually maintain the cytoplasmic differentiation typical for the normal squamous cells. Dyskaryosis may be described as mild, moderate, or severe. Another classification recognizes the superficial cell, intermediate cell, or parabasal cell dyskaryosis. Cytological examination of the smear fails to distinguish between parabasal cell dyskaryosis and carcinoma in situ, or between an intra-epithelial and an invasive lesion. (16 Refs)

8. TUMOR-SPECIFIC ANTIBODIES IN SERA FROM PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX. DETECTION BY A MEMBRANE IMMUNOFLUORESCENCE ASSAY ON CULTURED CERVICAL CARCINOMA CELLS.

van de Linde AW, Streefkerk M, Te Velde ER, Schuurman HJ, Szabo BG, Kater L
Div. Immunopathology, Dept. Internal Medicine and Pathology, Univ. Hosp., 101 Catharijnesingel, NL-3511 GV Utrecht, The Netherlands
Cancer Immunol Immunother; 11(3):201-206 1981

The possibility that circulating tumor-specific antibodies represent a diagnostic marker for the development of invasive cervical carcinoma (ICC) was studied. Sera were obtained from 74 patients with ICC, from 49 patients with early and preneoplastic stages (microinvasive carcinoma, carcinoma-in-situ, and dysplasia), from 65 controls without malignancy, and from 5 patients with non-ICC malignancies. Cervical cell carcinoma ME-180 cells were used as target cells. Sera were tested with an indirect immunofluorescence assay, by incubation with 0.1 mg/ml fluorescein-isothiocyanate (FITC)-labeled protein A which reacts with IgG or with FITC-labeled rabbit antihuman immunoglobulin antiserum diluted 1:30. Positive results were obtained from 63 (85%) of the ICC patients and 37 (57%) of controls. After absorption by tonsillar cells to remove non-specific antibodies, 61 (82%) of the ICC patients and 5 (8%) of the controls gave positive results. Patients with early and preneoplastic stages of cervical carcinoma did not differ significantly from controls. Evidently the antibody tested is specific for cervical carcinoma, but cannot be used as a diagnostic marker for early stages of the disease. Significance of the antibody in vivo is not known. (31 Refs)

9. LASER TREATMENT OF UTERINE CERVICAL LESIONS: RESULTS AFTER 18 MONTHS.

Coupez F, Legros R
Service de Gynecologie Chirurgicale et Obstetricale, C.H.I. Creteil, 94010 Creteil, France
Gynecologie; 32(1):57-61 1981

The results of CO2 laser treatment of 130 patients (99 reviewed and controlled) with cervix lesions is described. No infectious complications and only two hemorrhages were observed. Good results were obtained in 13/17 patients (16 reviewed and controlled) with carcinomas in situ or severe dysplasia, 9/12 (12 reviewed and controlled) with moderate to slight dysplasia with abnormal cytology, 48/67 (55 reviewed and controlled) with moderate to slight dysplasia with normal cytology, and 4/4 (4 reviewed and controlled) with papillomas and condylomas. The advantages and limitations of CO2 laser treatment of patients with cervix lesions are discussed. (6 Refs) (In FRE)

10. CRYOSURGICAL TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA.

Charles EH, Savage EW, Hacker N, Jones NC
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Charles R. Drew Postgraduate Medical Sch., Martin Luther King Jr. General Hosp., 12021 South Wilmington Ave., Los Angeles, CA, 90059
Gynecol Oncol; 12(1):83-88 1981

Over a 5-yr period from November 1973 to November 1978, 248 patients with abnormal cervical smears and satisfactory colposcopy were treated with cryosurgery following colposcopically directed cervical biopsy. Eighty-eight patients (35.5%) were lost to follow-up. Of the 160 patients followed, 134 (83.7%) were cured: 26 of the 160 (16.3%) were treatment failures. Although this cure rate is acceptable, this form of treatment should be used with caution in a clinic population because of the high percentage of patients lost to follow-up immediately following the procedure. (Author abstract) (28 Refs)

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11. A PRIMER ON TIME-DOSE FRACTIONATION FOR RADIATION THERAPY OF CARCINOMA OF THE CERVIX UTERI.

Hibbitts KR, Raeside DE, Adams GD, Bogardus CR
Dept. Radiological Sciences, Univ. Oklahoma Health Sciences Center, Oklahoma City, OK, 73106
Radiol Technol; 53(1):19-23 1981

Definition and tumor stage classification systems of carcinoma of the cervix are presented. A review of time-dose concepts as they apply to radiation therapy of carcinoma of the cervix uteri precedes discussion of the anatomy of the cervix and the pertinent radiation therapy. Optimization of radiation therapy regimes is placed in the context of the time-dose fractionation characterization. (11 Refs)

12. CARCINOMA OF THE UTERINE CERVIX STAGE III: A REPORT OF 311 CASES.

Hiilesmaa VK, Vesterinen E, Nieminen U, Grohn P
Dept. I and II Obstetrics and Gynecology, Helsinki Univ. Central Hosp., 00290 Helsinki 29, Finland
Gynecol Oncol; 12(1):99-106 1981

A series of 311 cases of carcinoma of the uterine cervix Stage III treated during 1964-1973 and followed up for at least 5 yr is presented. In 1964-1969 (Period I), local applications of radium were first given, followed by x-ray treatment of parametria with Muller's apparatus. This therapy was replaced in 1970-1973 (Period II) by external megavoltage treatment followed by radium applications. A total of 169 patients were treated in Period I and 142 in Period II. The 5-yr observed survival rate was 28% in the former and 36% in the latter period. The higher survival rate of the latter period was, however, statistically significant only in the first 2 yr after treatment. The relative survival rates for the older age groups of patients were better than those for the younger groups, a trend which was statistically highly significant. Megavoltage therapy increased the frequency of transient complications. Severe complications, however, were equally represented in both periods. Fistulas were observed in 12.5% of the patients. In 13% of the series a surgical operation was performed for correction of a complication. (Author abstract) (19 Refs)

13. MITOMYCIN-C, BLEOMYCIN, VINCRISTINE, AND CIS-PLATINUM IN THE TREATMENT OF ADVANCED, RECURRENT SQUAMOUS CELL CARCINOMA OF THE CERVIX.

Alberts DS, Martimbeau PW, Surwit EA, Oishi N
Section Hematology, Univ. Arizona Health Sciences Center, Tucson, AZ, 85724
Cancer Clin Trials; 4(3):313-316 1981

A combination chemotherapy regimen containing mitomycin-C (10 mg/m2, day 2), vincristine (0.5 mg/m2, days 1 and 4), bleomycin (30 U QD, days 1-4 as a continuous iv infusion during courses 1 and 2 only), and cis-platinum (50 mg/m2, days 1 and 22) was administered every 6 wk to 14 evaluable patients with advanced (ie, Stage IVB) and/or recurrent squamous cell carcinoma of the cervix. Four patients (29%) achieved a complete response, lasting 8, 9.5+, 17+, and 21+ mo. Three of these patients have had complete disappearance of their pulmonary metastases and one has had resolution of a large left-sided pelvic wall mass. Two additional patients (14%) had a partial response to therapy, each lasting 1.5 mo. The median survival for these 14 patients was 9.0 mo. The chemotherapy regimen was well tolerated. There were no drug-related deaths and no instances of severe or irreversible renal dysfunction or peripheral neuropathy. The mean lowest WBC and platelet counts were 4,540 and 00 per cubic mm, respectively. Although severe or life-threatening, thrombocytopenia occurred in only 36% patients, it appeared to be the dose-limiting toxicity of this drug combination. (Author abstract) (9 Refs)

14. CIS-PLATINUM IN TREATMENT OF ADVANCED OR RECURRENT SQUAMOUS CELL CARCINOMA OF THE CERVIX: A PHASE II STUDY OF THE GYNECOLOGIC ONCOLOGY GROUP.

Thigpen T, Shingleton H, Homesley H, Lagasse L, Blessing J
Gynecologic Oncology Group Headquarters, 1234 Market St., Suite 430, Philadelphia, PA, 19107
Cancer; 48(4):899-903 1981

Thirty-four patients with advanced or recurrent squamous cell carcinoma of the cervix no longer amenable to control with surgery and/or radiotherapy were treated with cis-platinum 50 mg/m2 iv every 3 wk. Among 22 patients who had received no prior chemotherapy, 3 complete and 8 partial responses were observed (response rate 50%), whereas only 2 partial responses were observed among 12 patients who had received prior chemotherapy (response rate 17%). The observed response rate was marginally sign ificantly higher among those with no prior chemotherapy ($p = 0.059$). The overall frequency of response was 38% (13/34). Responses were observed in those with pelvic (7/20) as well as extrapelvic disease (6/14). Adverse effects included primarily leukopenia (11/34), thrombocytopenia (13/34), nausea and vomiting (29/34), and azotemia (17/34). Adverse effects were generally mild to moderate and hence tolerable. Cis-platinum thus appears to be a highly active agent in the treatment of squamous cell carcinoma of the cervix at the dose and schedule tested. (Author abstract) (10 Refs)

15. INTRAARTERIAL CIS-PLATINUM IN THE MANAGEMENT OF SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX.

Carlson JA, Freedman RS, Wallace S, Chuang VP, Wharton JT, Rutledge FN
Dept. Obstetrics and Gynecology, Univ. Louisville Sch. Medicine, Ambulatory Care Building, 550 South Jackson St., Louisville, KY, 40292
Gynecol Oncol; 12(1):92-98 1981

Intraarterial cis-platinum was infused by hypogastric artery catheters in nine patients with squamous cell carcinoma of the uterine cervix. The dose of cis-platinum was 120 mg/m2 and the infusion was repeated at 4-wk intervals. Six patients had pelvic recurrences following radiation therapy and three had large-vol, primary cancers not amenable to conventional therapy. Three patients experienced partial tumor regression (greater than 50% reduction in measured diameters persisting for 3 mo), while six had progressive disease. Five patients achieved substantial palliation. Toxicity was similar to that seen with systemic administration. There were no significant catheter complications. (Author abstract) (23 Refs)

16. NEUROENDOCRINE CARCINOMA OF THE CERVIX: IMPLICATIONS FOR STAGING AND THERAPY.

Pazdur R, Bonomi P, Slayton R, Gould VE, Miller A, Jao W, Dolan T, Wilbanks G
Section Medical Oncology, Rush Univ., Chicago, IL, 60612
Gynecol Oncol; 12(1):120-128 1981

Ultrastructural examination of four cases of small carcinoma of the cervix demonstrated neuroendocrine granules. In each of these cases, distant metastases became evident within 3 mo of the initial diagnosis. The sites of metastases included liver, brain, bone marrow, and supraclavicular lymph nodes. Because of light microscopic, ultrastructural, and clinical similarities to pulmonary neuroendocrine carcinoma, three of these patients received combination chemotherapy effective in neuroendocrine tumors arising in the lung. One patient experienced remission of bulky pelvic tumor and supraclavicular metastases which lasted 11 mo. (Author abstract) (18 Refs)

17. THE EFFECT OF CONDOM USE ON SQUAMOUS CELL CERVICAL INTRAEPITHELIAL NEOPLASIA.

Richardson AC, Lyon JB
105 Collier Road, N. W., Suite 3080, Atlanta, GA, 30309
Am J Obstet Gynecol; 140(8):909-913 1981

Between January 1, 1968, and July 1, 1980, 377 of a total of 412 patients with biopsy-proven cervical intraepithelial neoplasia (CIN) were seen in the private office of the authors and followed for more than 6 mo after biopsy and the start of treatment. Thirty-five patients were lost to follow-up. Ninety-one were treated primarily by hysterectomy. The 286 patients in whom childbearing function was to be preserved were instructed, as soon as the diagnosis of CIN was confirmed, to use a mechanical barrier (the condom) throughout intercourse. In addition to the use of the condom, 40 of the 286 underwent surgical surgical conization and 107 underwent cryosurgery. All of these 147 patients eventually showed cytologic and colposcopic regression of the disease. One hundred and thirty-nine patients were treated with condom alone. One hundred and thirty-six of the 139 showed complete regression of the disease. Eighteen (6.2%) of the 286 patients had late recurrences of the disease; 12 of these experienced regression again with the resumption of the use of the condom. No patient showed progression of the disease while using the condom. All grades of CIN proved to be reversible. It is recommended that a mechanical barrier at intercourse be added to any program for conservative treatment of CIN. (Author abstract) (16 Refs)

18. CERVICAL CONDYLOMATOUS ATYPIA AND ITS RELATIONSHIP TO CERVICAL NEOPLASIA.

Ludwig ME, Lowell DM, Livolsi VA
(c/o Livolsi) 310 Cedar St., New Haven, CT, 06510
Am J Clin Pathol; 76(3):255-262 1981

Seven hundred fifty-six consecutive cervical biopsy specimens were obtained for abnormal Pap smear results or abnormality on physical examination to determine the incidence of condylomatous atypia (CLA) and its association with true dysplasia (cervical intraepithelial neoplasia; CIN). Histopathologic criteria for the diagnosis of CLA and its distinction from CIN were developed and are defined and illustrated. Clinicopathologic evaluation disclosed (1) CLA is often overdiagnosed as dysplasia; (2) cervical CLA is often associated with CIN in the same patient and may represent a potential precursor lesion; (3) CLA occurs more frequently than CIN in younger patients; and (4) the mean age of patients with pure CLA is younger than combined CLA-CIN, which is in turn younger than individuals with pure CIN. The results of this study are evaluated in light of induced squamous carcinoma and in view of the known association of condylomata and cancer of the external genitalia in humans. The results strongly indicate a need to examine the cervical CLA-CIN association with careful epidemiopathologic studies. (Author abstract) (45 Refs)

19. NUCLEAR AND CYTOPLASMIC OESTROGEN RECEPTORS IN SQUAMOUS CARCINOMA OF THE CERVIX.

Soutter WP, Pegorare RJ, Green-Thompson RW, Naidoo DV, Joubert SM, Philpott RH
Dept. Gynaecology, Univ. Sheffield, Jessop Hosp. for Women, Sheffield S3 7RE, England
Br J Cancer; 44(2):154-159 1981

Nuclear and cytoplasmic estrogen receptors (REN and REC) were sought in five normal cervices and in 43 specimens of squamous carcinoma of the cervix. All three tissue components of the five normal cervices contained both REN and REC. Thirty-five (81%) of the tumors contained receptors, but in only 9 (21%) were they found in both subcellular compartments. Twenty-four tumors (56%) had only REC and 2 had only REN. The potential therapeutic significance of these findings is not yet known, but it seems possible that tumors with an intact receptor mechanism might benefit from estrogen therapy and have a more favorable prognosis. (Author abstract) (19 Refs)

20. HISTOPATHOLOGIC DISTINCTIONS IN THE RELATIONSHIP OF ESTROGENS AND ENDOMETRIAL CANCER.

Horwitz RI, Feinstein AR, Vidone RA, Sommers SC, Robboy SJ
Robert Wood Johnson Clinical Scholar Program, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT, 06510
JAMA; 246(13):1425-1427 1981

The slides of 233 patients included in a case-control study of estrogens and endometrial cancer were reviewed to determine how often endometrial cancer was misdiagnosed and whether patients with uterine cancer had other coexistent endometrial diseases. Reasonably close agreements were found among the original diagnoses and those of three additional reviewers (the total range of disagreements among all pathologists was from 2% to 16%). Proliferative and hyperplastic endometrium coexisted in many specimens from patients with endometrial cancer, and especially in those who had used estrogen replacement therapy. In contrast, estrogen therapy had seldom been used by patients whose cancers were not accompanied by these proliferative and hyperplastic lesions. In addition, these changes were found significantly more often in women with Grade 1 cancers than Grade 2 or 3 cancers. We conclude from these data that diagnostic misclassification is uncommon and that coexistent proliferative and hyperplastic lesions occur frequently, especially among women with Grade 1 cancers. The data also suggest that the frequent finding of Grade 1 cancer in estrogen users is due to bleeding that results from the stimulated coexistent benign proliferating endometrium. (Author abstract) (12 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

21. THE PATHOLOGICAL ASSESSMENT OF OVARIAN NEOPLASMS. IV: THE SEX CORD-STROMAL TUMOURS.

Gee DC, Russell P

(c/o Russell) Dept. Gynaecological Histopathology, King George V Memorial Hosp., Missenden Road, Camperdown, New South Wales, Australia 2050

Pathology; 13(2):235-255 1981

All neoplasms of the ovary encountered in a 25-yr study period at the King George V Memorial Hospital were classified according to the World Health Organization (WHO) Histological Classification of Ovarian Tumors. Of just less than 1700 tumors, 168 fell into the category designated as sex cord-stromal tumors, this report analyzing their major clinical and pathological correlates. A detailed histological assessment is then presented, including 4 cases of the recently separated subcategory of sclerosing stromal tumor of the ovary. (Author abstract) (32 Refs)

22. NEUROHORMONAL PEPTIDE IMMUNOREACTIVE CELLS IN MUCINOUS CYSTADENOMAS AND CYSTADENOCARCINOMAS OF THE OVARY.

Sporrong B, Alumets J, Clase L, Falkmer S, Hakanson R, Ljungberg O, Sundler F

(c/o Falkmer) Dept. Pathology, Univ. Lund, Malmo General Hosp., S-21401 Malmo, Sweden

Virchows Arch [Pathol Anat]; 392(3):271-280 1981

In 144 benign mucinous cystadenomas of the ovary, 33 mucinous cystadenomas of borderline malignancy and 64 mucinous cystadenocarcinomas, the incidence of tumors containing argyrophil (and probably endocrine cells) was 18%, 33%, and 53%, respectively. The results of a semiquantitative assessment of the number of argyrophil cells in each individual tumor indicates that the greatest numbers occurred in the cystadenocarcinomas. As, however, the tumor cell density was larger in the cystadenocarcinomas than in the cystadenomas, and as the argyrophil cells often had a patchy distribution in the tumor epithelium, the incidence figures are unreliable. In addition, visualization of the argyrophil cells depends on an adequate fixation which is difficult to achieve in the routine processing of large tumor specimens. Many argyrophil cells in the cystadenocarcinomas displayed immunoreactivity with antisera raised against gastro-entero-pancreatic (GEP) neurohormonal peptides. In 10 such tumors immunohistochemical evidence was obtained for the presence of the following neurohormonal peptides in the tumor cells: somatostatin, glucagon, gastrin/CCK, neurotensin, and enkephalin. Four of these 10 cystadenocarcinomas were multihormonal, in that 3 contained two cell populations storing GEP neurohormonal peptides, and 1 tumor even three such populations. In the benign cystadenomas, however, no immunoreactive tumor cells were found. In those of borderline type, only two harbored immunoreactive cells. In both cases the tumor cells stored gastrin/CCK. The general appearance of the epithelium in the mucinous tumors - a continuous single-cell layer of mucin-producing cells interspersed with argyrophil cells of open type - and the spectrum of neurohormonal peptides observed, indicate an origin from the foregut endoderm. (Author abstract) (29 Refs)

23. SEROUS OVARIAN NEOPLASTIC AMYLASE (SONA): A POTENTIALLY USEFUL MARKER FOR SEROUS OVARIAN TUMORS.

van Kley H, Cramer S, Bruns DE

(c/o Bruns) Dept. Pathology, Univ. Virginia Medical Center, Charlottesville, VA, 22908

Cancer; 48(6):1444-1449 1981

A series of cystic ovarian tumors was studied with regard to amylase activity in the cyst fluid. Large amounts of amylase activity were present only in those patients with endosalpingeal-type lining epithelium (serous ovarian neoplasms). The amylase activity from two such patients was further characterized using G75 Sephadex chromatography, DEAE Sephadex chromatography, agarose gel chromatography, isoelectric focusing, and heat inactivation studies. Serous ovarian neoplastic amylase (SONA) exhibited properties different from amylases of pancreatic and salivary gland origin. SONA may be a useful biochemical marker in diagnosing and managing patients with serous ovarian neoplasms. (Author abstract) (40 Refs)

24. CHEMOTHERAPY OF ADVANCED OVARIAN EPITHELIAL CARCINOMA WITH MELPHALAN AND LEVAMISOLE: A PILOT STUDY OF THE GYNECOLOGIC ONCOLOGY GROUP.

Gusdon JP, Homesley HD, Muss HB, Heise ER, Herbst GA, Richards F, Spurr CL, Lovelace JV, Di Saia PJ

Dept. Obstetrics and Gynecology, Bowman Gray Sch. Medicine, 300 S. Hawthorne Road, Winston-Salem, NC, 27103

Am J Obstet Gynecol; 141(1):65-70 1981

Twenty-three patients with Stage III, Stage IV, or recurrent epithelial ovarian cancer were treated with a combination of melphalan and levamisole to determine a tolerable dosage schedule, possible adverse effects, and a general estimate of response rate and duration. In seven patients with measurable disease there were four complete responses (57%) with a median duration of 75 wk. Two of the complete responders have had negative second-look laparotomies while the other two patients have had subsequent progression. Of 16 patients with nonmeasurable disease, 2 have had negative second-look laparotomies and 2 remain progression free. Thus 8 of 23 patients (35%) had complete responses or remain progression free whereas 4 of 23 patients (17%) have had negative second-look laparotomies. No serious toxicity was encountered. Immunologic monitoring did not indicate significant immunologic reconstitution in these immunosuppressed patients. (Author abstract) (22 Refs)

25. HIGH-DOSE PLATINUM FOR THE TREATMENT OF REFRACTORY OVARIAN CANCER.

Bruckner HW, Wallach R, Cohen CJ, Deppe G, Kabakow B, Ratner L, Holland JF

Dept. Neoplastic Diseases, Mt. Sinai Sch. Medicine, 1 Gustave L. Levy Place, New York, NY, 10029

Gynecol Oncol; 12(1):64-67 1981

High-dose cis-diamminedichloroplatinum, 120 mg/m2, produced six clinical responses (3 complete) for 12 patients with advanced ovarian adenocarcinoma failing initial therapy with an alkylating agent. Responders survived 8+ to 20+ mo. the same dosage produced four (0 complete,1 short) responses for 20 patients refractory to a 50 mg/m2 dosage. Ten instances of nephrotoxicity and 5 of neurotoxicity were apparently related to a total cumulative dose of DDP and were predominantly seen in patients with prior DDP therapy and in patients with

maintained responses to high-dose DDP. (Author abstract) (8 Refs)

26. SURVEY OF CLINICAL BEHAVIOR OF PATIENTS WITH BORDERLINE EPITHELIAL TUMORS OF THE OVARY.

Nikrui N
Dept. Gynecology, Massachusetts General Hosp., Boston, MA, 02114
Gynecol Oncol; 12(1):107-119 1981

The present study analyzes the anatomical, pathological, and clinical elements in 62 cases of low potential malignancy of the ovary (25 mucinous, 36 serous, and 1 endometroid) from the Massachusetts General Hospital record room files from 1962 to 1979. Twenty-two serous tumors were Stage I, 6 were Stage II, 4 were Stage III, and 4 were recurrent. Among mucinous tumors twenty-one were Stage I, 1 was Stage III, 1 was Stage IV, and 2 were recurrent. Four patients had ascites: one patient's tumor was ruptured at surgery. The majority of cases were in Stage I. the av age was 54.5 yr. Thirty-seven percent of the cases were nulligravida. An abdominal mass was the most frequent finding and increased abdominal girth was the most frequent symptom. All of the patients were treated by excision of the tumor with or without hysterectomy. Chemotherapy followed surgery in 16 patients and radiation was used in 10 cases following surgery. Only one patient with early disease died of tumor. Five-yr survival was 91.4% among serous and 80.7% among mucinous. Ten-yr survival was 83.2% for serous and 73.4% for mucinous. (Author abstract) (23 Refs)

27. INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM IN PATIENTS WITH OVARIAN CARCINOMA.

Barker GH, Oriedge J, Wiltshaw E
Royal Marsden Hosp., Fulham Road, London SW3 6JJ, England
Br J Obstet Gynaecol; 88(7):690-694 1981

In a survey of 430 patients with ovarian cancer seen between 1969 and 1979, four patients (27-64 yr of age) with proven metastatic disease of the brain were found. The clinical details of these patients are presented and compared. In two patients, cisplatin may have prolonged their lives sufficientiy for the cerebral lesions to become apparent. Since survival is increased and new drugs do not affect tumor within the CNS, an increase in the incidence of CNS complications in the future is expected. (3 Refs)

28. ENDOLYMPHATIC STROMAL MYOSIS OF THE OVARY: A REPORT OF THREE CASES AND LITERATURE REVIEW.

Silverberg SG, Fernandez FN
Dept. Pathology, Univ. Colorado Sch. Medicine, Denver, CO, 80262
Gynecol Oncol; 12(1):129-138 1981

Three new cases of primary ovarian endolymphatic stromal myosis are added to six in the literature. This is a low-grade sarcoma of endometrial stromal origin, which may develop from ovarian endometriosis (present in 8 of the 9 cases reported), ovarian coelomic surface mesothelium or subcoelomic mesenchyme, or foci of 'benign stromatosis'. Eight of the nine reported cases have developed local or distant dissemination, and two have died of tumor. Follow-up, however, has been too short to predict the outcome of most cases, since one lesion first recurred after 15 yr, as is known to happen commonly in the more frequent uterine manifestation of this lesion. Treatment is primarily surgical, and progestational agents may be of value in recurrent disease. (Author abstract) (15 Refs)

29. TRENDS IN THE INCIDENCE OF ENDOMETRIOID AND CLEAR CELL CANCERS OF THE OVARY IN THE UNITED STATES.

Cramer DW, Devesa SS, Welch WR
Dept. Obstetrics and Gynecology, Brigham and Women's Hosp., Boston, MA, 02115
Am J Epidemiol; 114(2):201-208 1981

An increase in the reported incidence of endometrioid and clear cell cancers of the ovary occurred in the United States during the 1970s, while no change occurred in the overall incidence of ovarian cancer. The authors cannot rule out that this was due to a shift in the criteria for histologic classification or improved coding, although there seem unlikely to account entirely for the change. In the four areas where the trend for endometrioid and clear cell cancers of the ovary was examined, the percent increases in their occurrence were correlated with the percent increases in the occurrence of carcinoma of the uterine corpus. The concomitant trends and the biologic similarities between these histologic types of ovarian cancer and the uterine cancers suggest that common etiologic factors may be involved. The role of postmenopausal estrogen use in the etiology of ovarian cancer must be clarified by further epidemiologic studies, but such studies should take tumor histology into consideration. (Author abstract) (18 Refs)

TROPHOBLASTIC DISEASE

30. SPECIFIC ENZYME IMMUNOASSAY FOR HUMAN CHORIONIC GONADOTROPHIN.

Sekiya T, Furuhashi Y, Goto S, Kaseki S, Tomoda Y, Kato K
Dept. Obstetrics and Gynaecology, Nagoya Univ., Sch. Medicine, Nagoya, Japan
Acta Endocrinol (Kbh); 97(4):562-568 1981

A sandwich-type enzyme immunoassay system specific for human chorionic gonadotrophin (hCG) was prepared with the antibody Fab'-beta-D-galactosidase complex and the antibody F(ab')2-immobilized silicone rubber solid phase by using a purified antibody to beta subunit of hCG (hCGbeta). The assay system cross-reacted less than 4% with human luteinizing hormone (hLH) and human follicular stimulating hormone (hFSH), and proved to be highly sensitive with hCG measurable at levels as low as 0.3 mIU per assay tube. Using 50 ul of serum sample, 6-600 mIU/ml of hCG in serum could be determined specifically with the same degree of precision as in radioimmunoassay but without sample interference with the assay. The coefficients of variation within-run and between-run were 8.6-8.9%, and 4.9-10.7%, respectively. Values obtained with the enzyme immunoassay correlated well with those of radioimmunoassay ($r = 0.98$, slope = 0.94, y-intercept = 10.2 mIU/ml for 75 serum samples). Results of the immunoassay of hCG levels in serial samples of serum from healthy women and patients with choriocarcinoma show that this method is useful in the clinical diagnosis of trophoblastic disease. (Author abstract) (11 Refs)

31. OPERATIVE PROCEDURE AND INDICATIONS FOR SURGICAL MANAGEMENT OF PULMONARY METASTASIS OF CHORIOCARCINOMA.

Imaizumi M, Suyama M, Akiyama S, Kondo T, Kaseki S, Tomoda Y
Second Dept. Surgery, Nagoya Univ. Sch. Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya-shi, Aichi-ken 466, Japan
Jpn J Surg; 11(4):256-262 1981

Records of 19 patients (24-60 yr old) who underwent surgery for pulmonary metastases from choriocarcinoma were reviewed to assess the value of surgery and the possible relationship between human chorionic gonadotropin (hCG) titer and survival. Among 17 patients in whom urinary hCG titer was determined preoperatively, 3 showed marked elevation; all died of distant metastases postoperatively. In the remaining 14 patients, the titer was less than 1,100 milliUnit/ml, and in 10 of these patients, it was less than 200 milliU/ml. Thoracotomy was performed 21x in 19 patients, wedge resection 16x in 14 patients, and lobectomy 5x in the remaining 5 patients. Active trophoblastic cells were identified in 15 patients; the pulmonary lesion proved to be hematoma in the remaining 4 patients. Eight of nine patients with pulmonary choriocarcinoma showed a cellular response (ie, temporary increase in hCG titer in response to chemotherapy) preoperatively, whereas only one of the four with pulmonary hematoma showed such a response. If the preoperative hCG titer is low and a cellular response is present, surgical intervention should be considered. Since regional lymph node metastasis was not evident in any patient, extensive pulmonary surgery appears to be unnecessary. (9 Refs)

32. HLA ANTIGENS IN HUSBAND-WIFE PAIRS WITH TROPHOBLASTIC TUMOR.

Yamashita K, Ishikawa M, Shimizu T, Karoda M
Dept. Obstetrics and Gynecology, Asahikawa Medical Coll., Asahikawa, 078-11, Japan
Gynecol Oncol; 12(1):68-74 1981

Seventy-four patients with trophoblastic tumors (49: hydatidiform moles, 16: invasive moles, and 9 choriocarcinomas), 68 of their husbands (45, 15, and 8, respectively), and 76 controls were typed for HLA A and B specificities to determine whether or not there are specific HLA antigens associated with the occurrence of this tumor, and whether there is a relationship between the histocompatible combination of patient-husband and tumor growth. All subjects were Japanese. The results obtained were as follows: (a) No paternal and maternal HLA antigen was demonstrated to be associated with the tumor; (b) histocompatibility between patient and husband was not responsible for tumor growth. (Author abstract) (18 Refs)

MULTI-SITE STUDIES AND REVIEWS

33. EXPRESSION OF SILVER-STAINED NUCLEOLAR ORGANIZING REGIONS (AG-NORS) IN HUMAN CANCER.

Trent JM, Carlin DA, Davis JR
Dept. Internal Medicine, Cancer Center, Univ. Arizona, Tucson, AZ, 85724
Cytogenet Cell Genet; 30(1):31-38 1981

Five cases of ovarian adenocarcinoma, three cases of endometrial adenocarcinoma, and one case of transitional cell carcinoma of the bladder have been studied for expression of silver-stained nucleolar organizing regions (Ag-NORs). The modal chromosome number of these tumors varied from 37 to 72, with a wide range of chromosome numbers (13 to 150). The modal number of Ag-NORs in this sample varied from three to seven. Regression analysis among and between tumors demonstrated a proportionate increase in the number of Ag-NORs with increasing number of total chromosomes and increasing number of acrocentric chromosomes ($r = 0.64$ and 0.75, respectively). Modal assessment of Ag-NORs in both peripheral blood lymphocytes (PBLs) and cultured tumor cells in one patient revealed identical modes in normal and malignant cells. Also, no difference in the expression of Ag-NORs was observed between tumor cells obtained at biopsy and placed for 48 hr in agar culture and tumor cells established in finite monolayer culture. Our study provides further evidence for a proportionate increase in Ag-NORs with increasing numbers of acrocentric chromosomes and total chromosomes. (Author abstract) (22 Refs)

34. CURRENT STATUS OF THERAPEUTIC MODALITIES FOR TREATMENT OF GYNECOLOGIC MALIGNANCIES WITH EMPHASIS ON CHEMOTHERAPY.

Willson JK, Ozols RF, Lewis BJ, Young RC
(c/o Young) Medicine Branch, NCI, NIH, Bethesda, MD, 20205
Am J Obstet Gynecol; 141(1):81-98 1981

The current status of conventional therapies for gynecological malignancies is reviewed with special emphasis on the efficacy of chemotherapy. Detailed discussions are presented on the prognostic factors, surgical management, radiotherapy, chemotherapy, along with recommendations relative to ovarian cancer (including malignant germ cells tumors), carcinoma of the cervix, endometrial cancer and gestational trophoblastic disease. Radiotherapy in combination with surgery is the treatment of choice for malignant germ cell tumors of the ovary, carcinoma of the cervix, and low-risk Stage I endometrial cancer. The patients with advanced ovarian cancer, advanced carcinoma of the cervix who have para-aortic node metastases, advanced endometrial cancer, and uterine sarcoma who have an extrapelvic extension of the disease, high-grade histology, or metastases would benefit from aggressive postsurgical systemic therapy. Chemotherapy regimens containing bleomycin and mitomycin C were found to improve the survival of the patients with advanced cervical cancer. Progestational agents were used widely in the treatment of endometrial cancer: the efficacy of hormonal therapy was found to depend upon the progesterone affinity of the tumor. Drug regimens containing adriamycin and dacarbazine were the most effective in the patients with soft tissue uterine sarcomas. (199 Refs)

35. PHASE I CLINICAL STUDY OF BESTATIN.

Majima H, Suzuki M
Chiba Cancer Center Hosp., Nitona-cho, Chiba 280, Japan
Gan To Kagaku Ryoho; 8(2):278-284 1981

Bestatin, (2S,3R)-3-amino-2-hydroxy-4-phenylbutanoyl L-leucine, is a potent inhibitor of aminopeptidase B and leucine aminopeptidase, which increases delayed-type hypersensitivity reaction in aged mice and tumor bearing mice, and inhibits the growth of Gardner's lymphoma and IMC-carcinoma. The Phase I clinical study of bestatin in 38 patients with gynecological tumors indicates that the range of optimum oral daily dose of bestatin is from 30 to 100 mg, and that bestatin increases significantly lymphocyte number, absolute number of T cells and lymphocyte blastogenesis by concanavalin A at these dosages. The statistically significant trend of normalization was observed in some immunological parameters such as levels of

T cell, B cell, T gamma cell and lymphocyte blastogenesis by concanavalin A. No changes in immunoglobulin fraction is noted. So far no adverse reactions is noted in patients treated with bestatin at low dose of 30 mg daily up to 2 yr or at high dose from 300 to 900 mg daily for 1 or 4 wk. (Author abstract) (18 Refs) (In JPN)

36. IN UTERO EXPOSURE TO DES: WHAT HAVE WE LEARNED?

Noller KL
Dept. Obstetrics and Gynecology, Mayo Clinic, Rochester, MN, 55905
Mayo Clin Proc; 56(9):577-578 1981

The association between in utero exposure to diethylstilbestrol (DES) and the development of vaginal clear cell adenocarcinoma (CCA) in young women was first reported 10 yr ago. Subsequent studies indicated that cervical CCA was also related to DES but that these cancers occur only once in every several thousand exposed women. Benign abnormalities noted in DES exposed women included changes in the epithelium of the vagina and cervix and changes in the structure of the cervix and uterus. Because the epithelial changes (ie, metaplasia) mimic intraepithelial neoplasia, many women have been incorrectly diagnosed as having cervical dysplasia or carcinoma in situ. A large, multicenter DES project reported that these conditions occurred less frequently in the study cohort than in the unexposed controls. Infertility does not appear to be more frequent in DES-exposed women, but spontaneous abortion is slightly increased and premature delivery is increased. A pamphlet summarizing the documented effects of DES exposure has been prepared by the NCI. (10 Refs)

37. SEROEPIDEMIOLOGICAL STUDY OF HERPESVIRUS TYPE 2 AND CARCINOMA OF THE CERVIX.

Ohwada N
Dept. Obstetrics and Gynecology, Sch. Medicine, Gunma Univ., Maebashi-shi, Guma Pref. 371, Japan
Kitakanto Igaku; 31(2):87-97 1981

Sera obtained from patients with preinvasive and invasive cervical cancer, and ovarian and corpus cancer as well as from healthy control women were tested for neutralizing antibodies to herpesvirus type 1 (HSV-1) and type 2 (HSV-2) in regard to a possible association between HSV-2 and cervical cancer. Antibody titers to each virus type were determined simultaneously by a microtiter technique. The percentage of women with cervical cancer who had anti-HSV-2 antibody was significantly higher than that of patients with corpus and ovarian cancer and control women; cervical cancer patients 81%, corpus and ovarian cancer patients 26%, and control women 20%. However, the percentage of women having anti-HSV-1 antibody in the study group was comparable to that in the control group; cervical cancer patients 37%, corpus and ovarian cancer patients 39%, and control women 28%. The mean titer of neutralizing activity to HSV-2, as given by log2 of the reciprocal of the final serum dilution that exhibited the neutralizing activity, in the cervical cancer group (2.41 +-1.22) was also significantly higher than that in the corpus and ovarian cancer group (0.87 +-0.89) and in the control women (0.83 +-0.97). This difference was independent of age. It has been noticed that in some patients with cervical cancer, especially in the stage of carcinoma in situ, the neutralizing antibody titers decreased significantly after surgical resection o the cancer tissues. These findings suggest a strong association between HSV-2 infection and the establishment of cervical cancer, although it is not clear whether the virus has a causative role in the development of cervical cancer or not. (36 Refs) (In JPN)

38. IMMUNOPEROXIDASE LOCALIZATION OF PAPILLOMAVIRUS ANTIGENS IN CERVICAL DYSPLASIA AND VULVAR CONDYLOMAS.

Kurman RJ, Shah KH, Lancaster WD, Jenson AB
Dept. Obstetrics and Gynecology, Georgetown Univ. Hosp., 3800 Reservoir Road, Washington, DC, 20007
Am J Obstet Gynecol; 140(8):931-935 1981

Biopsies of 50 cases of cervical dysplasia (46 mild and 4 moderate) and 40 cases of vulvar condyloma acuminata (genital warts) were screened for the presence of papillomavirus antigens by means of a peroxidase-antiperoxidase method having immunospecificity against the genus-specific (common) antigen(s) of the papillomaviruses. With the use of this technique, on formalin-fixed, paraffin-embedded tissue, papillomavirus antigens were detected in cells with cytologic and histologic features of wart virus infection (so-called koilocytotic atypia). Cells showing a positive reaction for papillomavirus antigens were identified in 24 of 50 (48%) cases of cervical dysplasia and 20 of 40 (50%) cases of vulvar condyloma. The results of this study provide specific confirmation of the presence of papillomavirus antigens in cervical dysplasia and suggest that the papillomavirus may be an important factor in the etiology of this disease. (Author abstract) (18 Refs)

SELECTED PRE-CLINICAL STUDIES

39. CHROMATIN ANALYSIS IN HUMAN ENDOMETRIAL ADENOCARCINOMA BEFORE AND AFTER TREATMENT WITH 6-METHYL-17-HYDROXYPROGESTERONE ACETATE (MPA).

Barni S, Novelli G, Zanoio L, Gerzeli G, Vecchietti G
Istituto di Anatomia Comparata, Universita di Pavia, Piazza Botta 10, I-27100 Pavia, Italy
Virchows Arch [Cell Pathol]; 37(2):167-177 1981

Some molecular and ultrastructural characteristics of chromatin (propidium iodide intercalation into DNA during thermal denaturation. DNA content per nucleus and its hydrolysis kinetics, euheterochromatin ratio) were studied in the cells of endometrial adenocarcinomas following oral treatment with 6-methyl-17-hydroxyprogesterone acetate (MPA) at a dose of 1 g/day for 12 days. Ultrastructurally, before treatment the nuclei of tumor cells were often irregularly shaped and exhibited a mostly dispersed chromatin (euchromatin). In addition, the distribution of DNA content per cell was clearly abnormal, reaching ploidy levels of 16c. From a physicochemical standpoint, both the thermal denaturation and the HCl-hydrolysis of DNA revealed a high lability of chromatin. After progestin treatment, nuclear morphology appeared to approach normality, and large areas of heterochromatin reappeared which, after staining with propidium iodide, could be seen as strongly fluorescent points. DNA showed a higher resistance to thermal denaturation, especially evident at temperatures exceeding 70 C. Also the HCl-hydrolysis curves showed that, particularly with regard to short (less than 20 min) or protracted (greater than 140 min) hydrolysis times, DNA was less easily hydrolyzed than before MPA-treatment. A clearcut modification could be observed with regard to the DNA content per cell, high ploidy levels disappearing and values being less dispersed. On the whole, these findings demonstrated an effect of the drug on tumor cells, particularly affecting chromatin, at least with regard to the parameters examined. (Author abstract) (18 Refs)

40. EFFECT OF CIS-DICHLORODIAMMINEPLATINUM(II) ON CLONED OVARIAN ADENOCARCINOMA CELLS OF THE RAT IN VITRO.

Sekiya S, Iwasawa H, Yamauchi K, Kubota K, Takamizawa H
Dept. Obstetrics and Gynecology, Chiba Univ. Sch. Medicine, 1-8-1 Inohana, Chiba 280, Japan
Gynecol Oncol; 12(1):14-22 1981

Cloned rat ovarian adenocarcinoma cells (ROT58/C3) treated for 1 hr with 0.5 ug/ml or more of cis-dichlorodiammineplatinum(II) (DDP) or adriamycin (ADM) revealed a marked decrease in survival as estimated by the colony-forming method. Compared to cloned rat uterine adenocarcinoma cells (HTP/C1), the ROT58/C3 cells were more sensitive to the cytotoxic effect of both drugs. The survival of exponentially growing ROT58/C3 cells was reduced to less than 10% by a 0.5 ug/ml dose of DDP, as compared to a 1 ug/ml dose of ADM. Extensive morphological changes such as enlargement of the nuclear and nucleolar diameters, increase in the number of nucleoli, and the appearance of coarse and opaque chromatins were observed by optical and electron microscopy at as early as 48 hr after exposure to DDP for 1 hr. In addition, accumulation of cells at the G2 phase in the cell cycle was observed by flow microfluorometry. (Author abstract) (13 Refs)

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VAGINAL TUMORS

1. THE ROLE OF BRACHYTHERAPY IN THE TREATMENT OF PRIMARY CARCINOMA OF THE VAGINA AND FEMALE URETHRA.

Deicios L, Wharton JT, Fletcher GH, Rutledge FN
Dept. Radiotherapy, Univ. Texas Cancer Center, M. D. Anderson Hosp. and Tumor Inst., Houston, TX
Modern Interstitial and Intracavitary Radiation Management. George FW, ed. New York, Masson Publishing USA, Inc., Cancer Management, Vol. 6, 132 pp., 1981.

Treatment techniques for carcinoma in situ, squamous cell carcinoma of the vagina, adenocarcinoma of the vagina, and carcinoma of the female urethra are detailed. Previously published data for (1) primary carcinoma (99 squamous cell and 8 adenocarcinoma) of the vagina treated by irradiation (1948-1972), (2) clear cell adenocarcinoma of the vagina in young (1.5 to greater than 5 yr) females (1965-1976), and (3) carcinoma of the female urethra treated by irradiation (1948-1972) are presented. Epithelial tumors of the vagina and urethra can apparently be treated by external transvaginal, intracavitary, and interstitial irradiation with some success, regardless of age or stage and without the loss of vaginal function. (7 Refs)

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CERVICAL AND UTERINE TUMORS

2. LYMPHANGIOGRAPHY IN CERVICAL CARCINOMA. VIRCHOW'S NODE REVISITED.

Boyd WR, Baloga J, Dunbar RD, Toomey FB
Dept. Radiation Sciences, Loma Linda Medical Center, Loma Linda, CA
Appl Radiol; 10(5):92-93 1981

The case of a 67-yr-old woman with vaginal squamous carcinoma is presented. Bipedal lymphangiography showed filling defects of a left supraclavicular node that subsequent biopsy revealed to be a distant metastasis of the vaginal tumor. The accuracy of lymphangiographic findings in patients with carcinoma is quite good according to a review of the literature. The present case demonstrates the superiority of lymphangiography over physical examination for the identification of metastatic disease in the supraclavicular lymph nodes. (11 Refs)

3. HYSTEROSCOPIC EVALUATION OF PATIENTS WITH ABNORMAL UTERINE BLEEDING.

Valle RF
Dept. Obstretrics and Gynecology, Northwestern Univ. Medical Sch., Prentice Women's Hosp. Maternity Center, Chicago IL
Surg Gynecol Obstet; 153(4):521-526 1981

Abnormal uterine bleeding is the most common indication for dilation and curettage. Because of the pitfalls involved with this blind procedure, hysteroscopy was added for the evaluation of the patients in this study. In 419 premenopausal and 134 postmenopausal patients who had abnormal uterine bleeding, hysteroscopy was performed prior to dilation and curettage, and directed biopsies were obtained under hysteroscopic view when abnormal lesions were discovered. In 352 patients, an abnormality was hysteroscopically detected, such as endometrial polyps, submucous leiomyomas, intrauterine adhesions and focal lesions compatible with adenomatous hyperplasia or endometrial carcinoma, many of which were not detected at the subsequent dilation and curettage. Hysteroscopy provides a precise and accurate adjunct to traditional methods of diagnosing intrauterine abnormalities, particularly focal lesions which may be missed at curettage. (Author abstract) (8 Refs)

4. VALUE OF DUPLICATE SMEARS IN CERVICAL CYTOLOGY.

Davis JR, Hindman WM, Paplanus SH, Trego DC, Wiens JL, Suciu TN
Dept. Pathology, Univ. Arizona Health Sciences Center, Tucson, AZ, 85724
Acta Cytol (Baltimore); 25(5):533-538 1981

The cytologic accuracy, sources of error and value of duplicate samples were studied in 87 women simultaneously biopsied for cervical intraepithelial neoplasia. Separately evaluated by two laboratories, correlation with biopsy was 70% for the first cytology and 67% for the second. Discrepant cytologies were reciprocally reviewed in error analysis. The sources of error were cytologic sampling (10.9%), evaluation (5.8%) and both (4.0%). Attention is directed to the high proportion of cases (15%) in which sampling error was a factor; awareness of this observation is necessary in patient management. The duplicate second cytology was of substantial value in 7% of the cases and helpful in an additional 3.5%; both figures are lower than in recent reports. If errors in evaluation or evaluation sampling are held to a 10% level,, routine duplicate studies may not be justified. (Author abstract) (5 Refs)

5. SYRINGING AS A METHOD OF CELL DISPERSAL. II. EFFECT ON ABNORMAL CELLS.

Lopez PA, Cambier MA, Wheeless LL
Dept. Pathology, Univ. Rochester Medical Center, 601 Elmwood Ave., Rochester, NY, 14642
Anal Quant Cytol; 3(3):235-238 1981

The effect of shear forces generated by syringing was studied in gynecologic cell samples obtained by cervical scraping or endocervical aspiration. Cells collected were suspended in Mucosol and refrigerated for 1 wk before use. After control studies, aliquots of each sample were subjected to 35 strokes in an automatic device at varying pressures from 20-32 pounds/square inch (psi). A slide was made from each sample and 25 randomly selected fields were studied at 100x magnification using fluorescence microscopy. Abnormal cells were examined from squamous carcinoma, carcinoma in situ and dysplasias (nonkeratinizing [NK], mixed NK and metaplastic types). Overall cell loss and degree of dispersion were evaluated. In typical studies on samples from three ovarian adenocarcinomas, syringing at 20, 24, 28 and 32 psi resulted in persistence of abnormal cell groupings (often 4 or more) in most samples regardless of pressure. Although most samples exhibited some cell loss, the percentage of single abnormal cells was increased in 96% of the syringed samples. (11 Refs)

6. EVALUATION OF SINGLE-CELL CLASSIFICATION SCHEMES FOR COMPUTER CLASSIFICATION OF CERVICAL CELLS.

Poulsen RS, Oliver LH, Tousignant GT, Louis C
Dept. Pathology, McGill Univ., 3775 University Ave., Montreal, Quebec H3A 2B4, Canada
Anal Quant Cytol; 3(3):207-215 1981

Three single cell classification schemes were evaluated and compared with the performance of a cytotechnologist in classifying cells from routinely prepared cervical smears. The first, the standard quadratic subclass decision classifier (SQSDC) scheme, performed as well as the second (SQSDC with clustered subclasses). SQSDC also performed better than the third which employed a reject mechanism. The latter scheme has the added benefit of identifying cells most difficult to classify. All three schemes performed well in distinguishing normal squamous cells from significantly dysplastic cells or malignant cells. All three machine schemes performed poorly compared to the cytotechnologist in distinguishing abnormal squamous cells from nonsquamous cell types. The greatest difficulty with single-cell classification was with the smallest cell types, endometrial and small-cell carcinoma in situ. It is believed that some of this difficulty relates to use of 1 micron sample spacing for digitizing cell images. Current work proceeds with the use of a higher scanning resolution (0.7 micron sample spacing, 0.65 numerical aperture optics) and scanning cells in three colors (530, 570 and 620 nanometers). (6 Refs)

7. PROGRESS IN RADIO-ISOTOPE SURGERY FOR CERVICAL CARCINOMA.

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Zentralbl Gynaekol; 103(15):857-864 1981

The third phase in the use of radioisotopes for radical surgery of cervical carcinoma, using 99m Technetium antimony sulfide to localize pelvic lymph nodes on the operating camera table has yielded results which indicate good progress. The potency of lymphadenectomy was increased from an original

level of 52.5% to 81.6%. Recurrence mortality went down over the first 3 yr after treatment, according to preliminary results. (Author abstract) (11 Refs) (In GER)

8. BIOLOGICAL DOSES WITH TEMPLATE DISTRIBUTION PATTERNS.

Harrop R, Haymond HR, Syed AN, Feder BH, Neblett DL
Simon Fraser Univ., Burnaby, British Columbia, Canada
Modern Interstitial and Intracavitary Radiation Management. George FW, ed. New York, Masson Publishing USA, Inc., Cancer Management, Vol. 6, 132 pp., 1981.

A comparison is made of two brachytherapy treatments for cancer of the cervix, one involving the use of colpostats and tandem (treatment I) and the other involving the use of a Syed-Neblett template and tandem (treatment II). A common preceding external beam is assumed part of the total treatment plan in each case. Use of the template is associated with lateral infiltration of the tumor; loading of lateral needles enables doses near anatomical points B and elsewhere laterally to be raised substantially with little effect on doses to bladder and rectum. Suggested dose rate, time of application, and resulting dose at points A (medial region) and B and at bladder and rectum for treatmems I and II are given. Biological effect calculations for time dose fractionation (TDF), partial tolerance (PT), and cumulative radiation effect (CRE) are presented. The effect of changing from treatment I to treatment II is that TDF, PT, and CRE values obtained for point B are of the order of those originally obtained for point A. Biological effect is even more pronounced at point A: TDF units are 5x the corresponding effect at bladder or rectum although the dose is only 3x greater. Calculations made of biological effect components for 6 cases are shown; values illustrate changes that may follow therapy but do not account for choice of treatment I or II. Template use allows the possibility of differential loading. High TDF values at and near point A for treatment II do not seem to cause complications; the doses have been localized within tumor vol and are not associated with high bladder and rectum values. (29 Refs)

9. AN ANALYSIS OF THE SEVERE COMPLICATIONS OF IRRADIATION OF CARCINOMA OF THE UTERINE CERVIX: TREATMENT WITH INTRACAVITARY RADIUM AND PARAMETRIAL IRRADIATION.

Unal A, Hamberger AD, Seski JC, Fletcher GH
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Int J Radiat Oncol Biol Phys; 7(8):999-1004 1981

The results of therapy administered, according to new guidelines for the combination of intracavitary radium and external beam irradiation, to 254 patients (200 Stage IB, 50 Stage II-A, and 4 Stage II-B) with carcinoma of the uterine cervix are described. Patients were treated with either intracavitary radium and parametrial irradiation or 2,000 rad whole pelvis irradiation followed by intracavitary radium and parametrial irradiation. At 4 yr, 85.8% of patients were alive with no evidence of disease; only 6.3% of patients died of disease. The central failure rate was very low (6/254) and there were no pelvic failures when the primary tumor was controlled. All 6 central failures occurred in patients with Stage IB tumors (5 squamous carcinomas and 1 adenocarcinoma). The overall incidence of complications for all 254 patients was 7.5%. All complications occurred within 36 mo following treatment, except in one patient who developed small bowel obstruction 10 yr after irradiation. A correlation was observed between the incidence of complications and the amount of irradiation delivered. Complications (12 small bowel obstructions, 16 hydroureter hydronephrosis, 14 sigmoiditis, and 6 fistulae) were associated with a high number of mg hr of radium plus a high dose of external irradiation, in combination with either asymmetry of the radium system and/or history of previous pelvic inflammatory disease, pelvic surgery, or diverticulosis. (6 Refs)

10. HYPERBARIC OXYGEN THERAPY FOR CARCINOMA OF THE CERVIX: STAGES IIB LESS THAN IIIA, IIIB AND IVA: RESULTS OF A RANDOMIZED STUDY BY THE RADIATION THERAPY ONCOLOGY GROUP.

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Dept. Radiation Therapy-MS200, Hahnemann Medical Coll. and Hosp., 230 North Broad St., Philadelphia, PA, 19102
Int J Radiat Oncol Biol Phys; 7(8):991-998 1981

Optimal schedules using hyperbaric oxygen were compared with conventional treatment schedules of known value in the treatment of cervix carcinoma. Sixty-five stage IIB, IIIA, IIIB, and IVA patients were randomized to receive treatment either in air or in the hyperbaric chamber under three atmospheres of pressure. Of the 65 patients, 7 could not be evaluated. Of the 29 patients 'randomized to air,' 27 followed the prescribed course of external and intracavitary radiation. Only 19/29 patients 'randomized to hyperbaric oxygen' received all or most of the external treatment in oxygen. Over 90% of the patients were followed for 4 yr, 48/58 for 5 yr or more. In the Stage IIB group, only 1/9 local recurrences was found in the oxygen-treated group, 4/19 patients treated in air had local recurrences. Fifteen of the 29 air-treated and 14/19 oxygen-treated patients, including those living and those who had died of intercurrent disease or complications, showed no evidence of disease. Seven patients in each group of 29 patients developed complications. The results indicated no significant difference in survival between air-treated and oxygen-treated groups. The local tumor control rate was slightly better in those patients actually treated with oxygen but the number of patients with any element of failure was almost the same (24% in air and 26% in oxygen). (16 Refs)

11. PHASE II RANDOMIZED STUDY OF DOXORUBICIN, VINCRISTINE, AND 5-FU VERSUS CYCLOPHOSPHAMIDE IN ADVANCED SQUAMOUS CELL CARCINOMA OF THE CERVIX.

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Dept. Medicine, Div. Hematology/Oncology, Sch. Medicine, Univ. Alabama, 638 Zeigler Bldg., University Station, Birmingham, AL, 35294
Cancer Treat Rep; 65(9):901-903 1981

Sixty-one evaluable patients with advanced squamous cell carcinoma of the cervix were treated in a randomized fashion with either doxorubicin, vincristine, and 5-fluorouracil in combination (AVF) or with cyclophosphamide (CTX). Of 31 patients treated with AVF, only 3 (10%) responded (1 complete response and 2 partial responses). Of 30 patients treated with CTX, there were 2 (7%) with partial responses. Two patients responded to AVF after failing CTX; one patient responded to CTX after failing AVF. Neither of these regimens was predictably useful in our patient population. (Author abstract) (12 Refs)

12. LOCAL THERAPY OF CARCINOMA OF THE UTERINE CERVIX: PART 1.

Masuda H, Sumiyoshi Y, Shiojima Y, Suda T, Kikyo T, Iwata M, Fujiyama N, Machida Y, Nagai K
Dept. Obstetrics and Gynecology, Yokohama City Univ., Urafunecho, Minami-ku, Yokohama 232, Japan
Cancer; 48(8):1899-1906 1981

One-hundred-fifteen patients with cervical cancer were treated by placing bleomycin, carbazilquinone (Carboquone), and 5-fluorouracil suppositories in contact with cancer lesions located in the vaginal portion of the uterus or by inserting them into the cervical canal, twice a wk, 1 to 14x. The cancer lesions disappeared from 17 of 33 patients with Stage 0 lesions and 9 of 42 with Stage IA lesions. The remaining lesions were principally found in the deep portion of the cervical glands and tended to decrease the more often the suppositories were applied. This led to the presumption that if this local therapy had been carried on longer it would be eradicated even the remaining lesions from the patients with Stage 0 and IA lesions. The optimal per administration dose of bleomycin appeared to be 30 mg. The use of Witepsol (Dynamit Nobel Aktiengesellschaft, FRG) suppository base was accompanied by frequent adverse reactions to it, which hindered the local therapy from being repeated over long periods of time. An equal amount mixture of hydroxypropyl cellulose and carbomer (Carbopol 934) as the suppository base was accompanied by relatively less adverse reactions, which permitted the prolonged local therapy with the suppositories. A trace of bleomycin was also found in the ovaries, but it did not cause microscopically evident histologic changes, nor did it affect the menstrual cycle. If early cancer can be treated completely by local therapy, it will be useful for the younger patient with early cervical cancer. (Author abstract) (14 Refs)

13. CIS-PLATINUM IN GYNECOLOGIC CANCER. II. SQUAMOUS CELL CARCINOMA OF THE CERVIX.

Hall DJ, Diasio R, Goplerud DR
Dept. Obstetrics and Gynecology, Univ. Tennessee Coll. Medicine, 1924 Alcoa Highway, U-27, Knoxville, TN, 37920
Am J Obstet Gynecol; 141(3):305-308 1981

Twenty-eight patients with squamous cell carcinoma of the cervix and 1 patient with squamous cell carcinoma of the vagina were treated with cis-dichlorodiammineplatinum at a dose of 60 mg/m2. Of these patients, 22 were evaluable. No patient had a complete response, two (9%) had partial responses, nine (41%) had stable disease, and 11 (50%) had progressive disease. The overall response rate was 9%. (Author abstract) (no Refs)

14. UTERINE SARCOMAS: AN ANALYSIS OF 69 PATIENTS.

Mantravadi RV, Bardawil WA, Lochman DJ, Liebner EJ, Townsend DE, Chao JH, Chaudhuri B
Univ. Illinois Hosp., P.O. Box 6998, Chicago, IL, 60680
Int J Radiat Oncol Biol Phys; 7(7):917-922 1981

In a review of 69 uterine sarcomas, histological types included 32 leiomyosarcomas (LMS), 10 endometrial stromal sarcomas (ESS), 5 rhabdomyosarcomas (RMS), 14 mixed mesodermal sarcomas (MMS), and 3 fibrosarcomas (FS). Staging by International Federation of Obstetrics and Gynecology standards indicated 29 stage I, 5 stage II, 11 stage III, 7 stage IV, and 17 unknown. Procedures employed included total abdominal hysterectomy and bilateral salpingooophorectomy in 54, surgery alone in 31, radiotherapy (RT) alone in 15 , preoperative RT and surgery in 5, and surgery followed by RT in 18. The overall survival rate was 50.7% after 2 yr and 37.9% after 5 yr. The 5-yr survival rate was 17/29 (58%) for Stage I, 2/5 (40%) for Stage II, and 0/11 for Stage III and 0/7 for Stage IV. At any given stage patients with LMS showed bett er survival rates than other histologic types. Combined treatment produced the lowest rate of pelvic failures. Distant metastases occurred in 73.3% of cases; common metastasis sites were lung and liver. Lung metastases occurred in all LMS patients showing failure. Adjuvant postoperative radiotherapy was recommended in LMS later than stage I and in all stages of other types. Systemic chemotherapy was also recommended as part of comprehensive treatment. (16 Refs)

15. WORKSHOP I: CURRENT AND FUTURE HORMONE SUPPLEMENT THERAPY. 6. ESTROGEN SUPPLEMENT THERAPY DURING THE MENOPAUSAL PERIOD.

Aono T, Minemikawa J
Dept. Obstetrics and Gynecology, Osaka Univ. Sch. Medicine, Osaka, Japan
Nippon Naibunpi Gakkai Zasshi; 57(3):337-340 1981

In conjunction with a discussion on selecting appropriate candidates for estrogen supplemental therapy and constructing a treatment schedule, the use of estrogen therapy by Japanese women and results of a survey on its relationship to occurrence of uterine endometrial cancer are reported. The proportion of endometrial cancer incidence to cervical cancer incidence among women in America and Europe is thought to be about 1:1, while that in Japan is thought to be about 1:10. A matched pair analysis of 72 women who had uterine endometrial cancer and 72 women who did not have cancer (controls) revealed 19 matched pairs cross-categorized as estrogen-using cancer patients and estrogen-nonuser controls, and 8 pairs matching non-estrogen using cancer patients and estrogen-using controls. Thus, the relative risk of women who use estrogen of having uterine endometrial cancer was 19/8 (2.38). Because patients who used gestagen with the estrogen had a lower relative risk of having uterine endometrial cancer than those who were administered estrogen alone, this combination is recommended. Short term + least necessary dose treatment with estrogen, combining estrogen and gestagen, and careful monitoring of women who use estrogen for 1-2-yr intervals are recommended. (4 Refs) (In JPN)

16. HERPESVIRUS TYPE 2 IN ADENOCARCINOMA OF THE UTERINE CERVIX: A POSSIBLE ASSOCIATION.

Menczer J, Yaron-Schiffer O, Leveston-Kriss S, Modan M, Modan B
Dept. Gynecology, Chaim Sheba Medical Center, Tel Hashomer, Israel
Cancer; 48(7):1497-1499 1981

Sera from 16 Jewish patients with histologically confirmed adenocarcinoma of the uterine cervix (AUC) and 32 control subjects matched by age and ethnic origin were examined for herpesvirus Type 1 (HSV-1) and Type 2 (HSV-2) neutralizing antibodies. Titers were determined by means of the quantitative plaque reduction neutralization test on VERO cell monolayers, using HSV-1 strain VR3 and HSV-2 strain. Significantly increased levels of antibodies against both virus strains were found in the AUC patients as compared with the controls. The trends in the AUC series resembled those in a previous similar case-control study of squamous cell carcinoma of the uterine cervix (SUC). Thus, the previously observed association between HSV-2 and SUC is true for AUC as well, despite differences in the clinical and epidemiologic characteristics of the two malignancies. (Author abstract) (9 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

17. LYMPHOGENIC METASTASES OF MALIGNANT OVARIAN NEOPLASMS.

Iurkova LE
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Vopr Onkol; 27(8):87-98 1981

Current clinical data on the lymphatic metastases of ovarian cancer are reviewed. Postmortem examinations showed lymphogenic metastases in 50-80% of the patients with ovarian cancer. Metastatic involvement of para-aortal lymph nodes was recorded in 29.7% of the patients, while involvement of the pelvic lymph nodes was diagnosed only in 10.8%. Involvement of para-aortal lymph nodes was recorded in 20% of the patients with Stage I, in 40% with Stage II, and in 70% with Stage III. The diagnostic accuracy of lymphography depends upon the interpretation of the pathologic changes of the lymph node. (105 Refs) (In RUS)

18. ADENOCARCINOMA OF THE UTERINE TUBE: POTENTIAL FOR LYMPH NODE METASTASES.

Tamimi HK, Figge DC
Dept. Obstetrics and Gynecology, Univ. Washington, RH-20, Seattle, WA, 98195
Am J Obstet Gynecol; 141(2):132-137 1981

A clinicopathologic study of 15 cases of primary adenocarcinoma of the uterine tube occurring over a 12-yr period is presented. The mean age of the patients was 54.8 yr. Predominant symptoms were abnormal bleeding, abnormal vaginal discharge, and pelvic pain. Abnormal vaginal cytology was noted in two instances (13%). A pelvic mass was detected in two thirds of the patients. The neoplasm was bilateral in three instances (20%). Lymph nodes were involved in eight cases (53%), and metastatic spread to the para-aortic nodes was present in five (33%). The most common primary treatment was total abdominal hysterectomy and bilateral salpingo-oophorectomy. Various combinations of adjuvant radiation therapy and chemotherapy were also employed. Six patients (40%) are alive without evidence of recurrent cancer. It is concluded that lymphatic spread, especially to the para-aortic nodes, is a major pattern dissemination for adenocarcinoma of the uterine tube. The presence of tumor in capillary-like spaces bears a strong relationship to lymph node metastases, and the para-aortic nodes are a frequent site of involvement even when the disease is apparently limited to the tube. (Author abstract) (12 Refs)

19. GRANULOSA THECA CELL TUMORS IN PREMENARCHAL GIRLS: A CLINICAL AND PATHOLOGIC STUDY OF TEN CASES.

Lack EE, Perez-Atayde AR, Murthy AS, Goldstein DP, Crigler JF, Vawter GF
Dept. Pathology, Children's Hosp. Medical Center, 300 Longwood Ave., Boston, MA, 02115
Cancer; 48(8):1846-1854 1981

Granulosa theca cell tumor (GTCT) in the premenarche accounted for 7% of all ovarian tumors treated at the Children's Hospital Medical Center from 1928 through 1979. The av age of the 10 girls at the time of diagnosis was 5 yr (range 11 mo-12 1/2 yr) with precocious 'pseudopuberty' and an abdominal mass being the most common presentation. GTCTs were solitary (5 right, 5 left) with an av diameter of 12.1 cm. Histologic examination showed a predominantly diffuse or solid pattern with prominent luteinization; Call-Exner bodies and folded ('coffee-bean') nuclei were inconspicuous. Ultrastructural examination of one GTCT confirmed the presence of both granulosa and theca components with the latter showing extensive luteinization; estradiol, testosterone and prolactin were demonstrated in the same tumor using immunologic techniques. The av follow-up time was 21 yr with 9 of the 10 patients being followed for more than 10 yr. Salpingo-oophorectomy resulted in cures despite the occurrence of tumor spillage in two patients. The prognosis for GTCTs in the premenarche appears more favorable than for those occurring in adulthood, but further study is needed to completely define their full biologic potential; the significance of subsequent breast cancer in two long-term survivors merits further investigation as well. (Author abstract) (24 Refs)

20. OVARIAN ENDOMETRIOID ADENOFIBROMATOUS AND CYSTADENOFIBROMATOUS TUMORS: BENIGN, PROLIFERATING, AND MALIGNANT.

Roth LM, Czernobilsky B, Langley FA
Dept. Pathology, Indiana Univ. Sch. Medicine, 1100 W. Michigan St., Indianapolis, IN, 46223
Cancer; 48(8):1838-1845 1981

Ovarian endometrioid tumors with an adenofibromatous pattern have been described but the entire spectrum of these tumors has not been analyzed. A series of 10 cases was studied and divided into 2 benign, 4 proliferating, and 4 malignant tumors on the basis of their morphologic characteristics. The most useful criterion for distinguishing proliferating from benign adenofibromatous tumors is increased epithelial proliferation, associated with glandular complexity and crowding in the former. Proliferating tumors may represent one form of the endometroid tumor of borderline malignancy. The presence of a confluent growth pattern with invasion of the stroma distinguishes malignant from proliferating tumors. The various tumors in this group frequently show squamous metaplasia and are often associated with endometriosis. Because of the relatively small series, the biologic behavior of these histologic variants cannot be evaluated at this time. (Author abstract) (20 Refs)

21. PROLIFERATIVE AND MALIGNANT BRENNER TUMORS. REVIEW OF 47 CASES.

Woodruff JD, Dietrich D, Genadry R, Parmley TH
Dept. Gynecology and Obstetrics, Johns Hopkins Hosp., Baltimore, MD, 21205
Am J Obstet Gynecol; 141(2):118-125 1981

The Brenner tumor has been promoted as a relatively rare benign ovarian neoplasia. During the past three decades, the recognition of 'malignant' and 'proliferating' variants has produced controversy and conflict as to the histopathologic criteria for definite diagnosis of these lesions and, more importantly, as to their relationship to 'the controversial ovarian tumor.' The opportunity to study 47 cases of malignant and proliferative Brenner tumors is the subject of this article. Histopathologic criteria for diagnosis, histogenesis, and clinical significance of these unique tumors are discussed. (Author abstract) (16 Refs)

22. CLASSIFICATION SYSTEMS.

Ulfelder H
Harvard Medical Sch., Massachusetts General Hosp., Fruit St., Boston, MA, 02114
Int J Radiat Oncol Biol Phys; 7(8):1083-1086 1981

Current staging classification for ovarian neoplasms is reviewed. It was emphasized that although the system fails to identify so-called borderline tumors or to assess properly the prognostic value of cytologic examination of the ascitic fluid or peritoneum, it is able to classify the majority of cases into histologic and morphologic subgroups of prognostic significance. (4 Refs)

23. THE VALUE OF TUMOR MARKERS IN CANCER OF THE OVARY.

Cantarow WD, Stolbach LL, Bhattacharya M, Chatterjee SK, Barlow JJ
(c/o Stolbach) Pondville Hosp., P.O. Box 111, Walpole, MA, 02081
Int J Radiat Oncol Biol Phys; 7(8):1095-1098 1981

Tumor markers identified in the patients with ovarian cancer are reviewed. Current list of markers includes ovarian cystadenocarcinoma-associated antigen, galactosyltransferase, cystine aminopeptidase, carcinoplacental alkaline phosphatase, carcinoembryonic antigen, alpha-fetoprotein, and human chorionic gonadotropin. Although these markers fail to meet the criteria for early detection of ovarian cancer, they can be used in the immunodetection, monitoring of the therapy, and possibly in the immunotherapy. (35 Refs)

24. FREQUENCY OF AN ALLELE FOR LOW ACTIVITY OF ALPHA-L-FUCOSIDASE IN SERA: POSSIBLE INCREASE IN EPITHELIAL OVARIAN CANCER PATIENTS.

Barlow JJ, DiCioccio RA, Dillard PH, Blumenson LE, Matta KL
Dept. Gynecologic Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263
JNCI; 67(5):1005-1009 1981

Sera from a group of patients with ovarian cancer had a statistically significant deficiency of alpha-L-fucosidase activity compared with sera from healthy females or female patients with cervical or breast cancer. Mixing experiments did not identify an inhibitor of alpha-L-fucosidase activity in the sera of ovarian cancer patients. Decreased activity of alpha-L-fucosidase was not associated with stage of disease, tumor burden, histologic type, or grade of differentiation. Unlike alpha-L-fucos idase, beta-mannosidase and beta-N-acetylglucosaminidase in sera of ovarian cancer patients were not deficient in activity. Examination of population data of healthy females and of pedigrees of ovarian cancer patients suggested that the quantitative activity of alpha-L-fucosidase in serum was genetically determined. Of 60 healthy females, 4 had low enzyme activity (less than 100 U alpha-L-fucosidase/ml serum), 26 had intermediate activity (100-274 U alpha-L-fucosidase/ml), and 30 had high activity (275 U/ml), whereas of 44 ovarian cancer patients, 11 had low, 29 had intermediate, and 4 had high activity. Application of the Hardy-Weinberg law to these data revealed that low enzyme activity in sera was 3x more prevalent in the ovarian cancer group, the allele for this low enzyme activity being 2x more common. These observations suggested that deficiency of alpha-L-fucosidase activity in sera of females may be a hereditary condition associated with increased risk for development of ovarian cancer. (Author abstract) (11 Refs)

25. HETEROCHROMATIN POLYMORPHISM OF A1 CHROMOSOME IN PATIENTS WITH OVARIAN CARCINOMA.

Adomat W, Weise W
Landesfrauenklinik der Medizinischen Akademie Magdeburg, Gerhart-Hauptmann-Str. 35, DDR-3010 Magdeburg, E. Germany
Zentralbl Gynaekol; 103(15):865-873 1981

Studies conducted by Atkin and Pickthall are likely to suggest more frequent occurrence in normal cells of enlargement of the heterochromatin region of the A1 chromosome in patients with ovarian carcinoma, and it is also claimed to be a predisposing factor, in the context of ovarian carcinoma. - The authors of this paper have tried to find out, if they could draw similar conclusions from their own patients and, therefore, applied cytogenetic tests of lymphocytes to 50 patients, including 25 who had undergone treatment for ovarian carcinoma and 25 control probands. - An assessment was made of 298 mitoses. C-bands were accurately measured and calculated in 84 mitoses of both groups. - The dimensions of A1 heterochromatin were variable in the authors' preparations, too. However, such variability in size in either group is considered still as normal variant of the well-known A1 polymorphism, and the authors were not convinced that pathognomonic relevance should be attributed to those findings. - Enlarged C-band of A1 chromsome was recordable only from one lymphocyte culture of one patient with ovarian carcinoma. C-banding, consequently, cannot be considered a suitable screening method for ovarian carcinoma, in the context of lymphocyte culturing. (Author abstract) (10 Refs) (In GER)

26. CIS-PLATINUM IN GYNECOLOGIC CANCER. I. EPITHELIAL OVARIAN CANCER.

Hall DJ, Diasio R, Goplerud DR
Dept. Obstetrics and Gynecology, Univ. Tennessee Coll. Medicine, 1924 Alcoa Highway, U-27, Knoxville, TN, 37920
Am J Obstet Gynecol; 141(3):299-304 1981

Eighteen patients with epithelial ovarian cancer were treated with cis-dichlorodiammineplatinum at a dose of 60 mg/m2. There were two (11%) complete responses, seven (38%) partial responses, seven (38%) with stable disease, and two (11%) with progressive disease. The overall response rate was 49%. In nine patients previously untreated, there was an overall response rate of 66.6% (6 of 9). (Author abstract) (11 Refs)

27. PROGESTIN THERAPY FOR ADVANCED OVARIAN CANCER: A PHASE II EASTERN COOPERATIVE ONCOLOGY GROUP TRIAL.

Slayton RE, Pagano M, Creech RH
Section Medical Oncology, Dept. Internal Medicine, Rush Medical Coll., 1725 W. Harrison St., Chicago, IL, 60612
Cancer Treat Rep; 65(9):895-896 1981

Medroxyprogesterone acetate was administered to 19 patients no longer responding to surgery, radiation therapy, or conventional cytotoxic chemotherapy. Dosage was 1,000 mg im daily for 8 wk, or longer if no tumor progression was noted. Performance status was classifies as Grade 0 (fully active), Grade 1 (able to do light work), grade 2 (ambulatory, but unable to do work), Grade 3 (capable of limited self-care, confined to bed or chair), or Grade 4 (incapable of self-care, confined to bed or chair). No patients of Grade 4 were accepted. Of the patient tested there were one Grade 0, nine Grade 1, five Grade 2, and four Grade 3. Regression was defined as 50% or greater decrease in the products of the perpendicular diameters of measurable lesions. Progression was defined as

25% or greater increase over original measurements, or the appearance of new tumors. No response to treatment was noted in any case. Median survival was 2 mo, with 75% dying within 4 mo. Restriction of trial use of progestin therapy to patients with endometrioid histology is recommended. (10 Refs)

28. ORAL CONTRACEPTIVES AND RISK OF OVARIAN CANCER.

Willett WC, Bain C, Hennekens CH, Rosner B, Speizer FK
Channing Lab., Harvard Medical Sch., 180 Longwood Ave., Boston, MA, 02115
Cancer; 48(7):1684-1687 1981

Among a large cohort of married, female, registered nurses under 55 yr of age, oral contraceptive (OC) use was examined in women with ovarian cancer and 470 age-matched controls. Use of OCs before the diagnosis of cancer was reported by 28% of the women with ovarian cancer and 33% of the controls, yielding a relative risk of 0.8 (95% confidence limits 0.4-1.5). This apparent inverse relationship was attributable to a large effect in women 35 yr of age or younger (relative risk = 0.2, 95% confidence limits 0.1-1.0). Patients with ovarian cancer were 2.2 times more likely than controls to be nulliparous. These data provide reassurance that OC use is not likely to be associated with any major increase in risk of ovarian cancer, but suggest that future studies of this relationship need to consider the possible confounding effect of infertility. (Author abstract) (12 Refs)

29. AN EPIDEMIOLOGIC STUDY OF EPITHELIAL CARCINOMA OF THE OVARY.

Hildreth NG, Kelsey JL, LiVolsi VA, Fischer DB, Holford TR, Mostow ED, Schwartz PE, White C
(c/o Kelsey) Dept. Epidemiology, Yale Univ. Sch. Medicine, P.O. Box 3333, New Haven, CT, 06510
Am J Epidemiol; 114(3):398-405 1981

A case-control study to identify risk factors for epithelial ovarian cancer was undertaken among women in the age group 45-74 yr who had been admitted to seven hospitals in Connecticut between July, 1977, and March, 1979. Characteristics that were found to increase the risk of epithelial ovarian cancer included being white, never having been pregnant, having a late age at menopause, having a family history of cancer of the ovary or endometrium, and having a long estimated number of yr of ovulation. Prior use of postmenopausal estrogens did not alter the risk for epithelial ovarian cancer, but there was some indication that oral contraceptives protect against ovarian cancer. Women with ovarian cancer were somewhat more likely to have had a history of an underactive thyroid and were somewhat less likely to have had a history of an overactive thyroid than controls, although these trends were not statistically significant. (Author abstract) (20 Refs)

TROPHOBLASTIC DISEASE

30. CORRELATION BETWEEN THE INDICES OF TROPHOBLASTIC BETA-1-GLOBULIN, CHORIONIC GONADOTROPIN AND CLINICAL COURSE OF THE DISEASE IN PATIENTS WITH UTERINE CHORIOEPITHELIOMA.

Zhordania KI, Sokolov AV, Kadagidze ZG, Molodyk AA
Cancer Res. Center, Moscow, USSR
Akush Ginekol (Mosk); (7):55-56 1981

The blood level of trophoblastic beta-1-globulin (TBG) and urinary secretion of chorionic gonadotropin (HCG) were monitored in 30 patients undergoing polychemotherapy for uterine chorioepithelioma. Effective therapy was correlated with the decrease of TBG and HCG levels, while development of metastases and dissemination of the primary tumor was associated with the increase of TBG and HCG levels. (3 Refs) (In RUS)

31. DISSOCIATION OF CHORIOADENOMA DESTRUENS FROM HYDATIDIFORM MOLE BY URINARY STEROID ANALYSIS.

Kodama M, Kodama T, Totani K
Aichi Cancer Center, Res. Inst., Nagoya, Japan
Am J Obstet Gynecol; 141(3):288-293 1981

Dissociation between hydatidiform mole (HM) and chorioadenoma destruens (CA) was attempted by gas chromatographic analysis of urinary steroids. In the chromatogram, Fraction 2 (F2) including four pregnane steroids (17-hydroxypregnenolone, pregnenolone, pregnanediol, and pregnanetriol) reflected the biologic activity of molar human chorionic gonadotropin (hCG), and the ratio of F2 to Fraction 1 (F1) (17-ketosteroids) was found useful in monitoring secondary growth of trophoblastic tumor: Urinary log F2/F1 after curettage declined quickly and unidirectionally in HM, but the same parameter exhibited a temporal rise in CA at 11 to 20 days after curettage because of the molar hCG from residual tumor tissue. The resolution between HM and CA at that stage (11 to 20 curettage days) was of the order of diagnostic use and superior to that with immunoreactive hCG. The data obtained are discussed in the light of pathophysiology of CA. (Author abstract) (15 Refs)

MULTI-SITE STUDIES AND REVIEWS

32. LYMPH SCAN WITH RADIONUCLIDES IN GYNECOLOGIC TUMORS..

Tang J, Chen S, Zhang Y, Zhang X, Yu G, Liu Z
Isotopes Unit, Ritan Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Zhonghua Zhonglin Zazhi; 3(1):42-45 1981

Radionuclide scanning of lymphatics using Au-198 colloids is described for 40 of 224 cases studied between 1976 and 1978. There were 35 cases of recurrent squamous carcinoma of the cervix, 2 cases of recurrent ovarian carcinoma, 1 case of recurrent squamous carcinoma of the vulva and 2 others. In 30 of the 40 cases renography were simultaneously performed. The positive diagnostic rate for lymphatic scintigraphy was 27/30 while that for renography was 20/30, showing that the diagnostic conformation rate was higher for lymphatic scinti-

graphy. The positive rate was raised to 29/30 when the two technics were combined. The overall positive rate in the sence was 37/40. It is concluded that lymphatic scanning with radionuclides is a simple and noninvasive method that can be repeatedly used to evaluate treatment results and in patient follow-up. Changes in the lymph scan can also reflect lymphatic functions. The limitation of this technic is that it produces a rougher picture of the lymphatics as compared to lymphography with iodized oils and gives certain number of false negative results. Three illustrative cases are given, and the technic is discussed. (11 Refs) (In CHI)

33. ENDOMETRIAL STROMAL TUMORS OF EXTRA-UTERINE TISSUE.

Ulbright TM, Kraus FT
(c/o Kraus) Dept. Pathology, St. John's Mercy Medical Center, 615 South New Ballas Road, St. Louis, MO, 63141
Am J Clin Pathol; 76(4):371-377 1981

Three extra-uterine tumors, unassociated with endometriosis, had light microscopic features of endometrial stromatosis (low-grade endometrial stromal sarcoma). Two tumors occurred in the retroperitoneum and one adjacent to the vagina. Distinctive features identifying these neoplasms as ectopic growths of endometrial stroma included prominent vessels with concentric whorls of tumor cells, foam cells, eosinophilic hyaline globules, bland cytologic features, and rare mitoses. The ultrastructure of one of the tumors was typical of endometrial stroma. Infiltrative margins and analogy with endometrial stromatosis make late recurrence likely unless excision margins are adequate. The postulated histogenesis of the tumors is mesothelial and mesenchymal cells of pelvis and retroperitoneum. Pre-existing endometriosis of ectopic ovary is possible but unnecessary. Recognition of the distinctive pattern of these slow-growing tumors should prevent confusion with more aggressive sarcomas. (Author abstract) (31 Refs)

34. SMOOTH-MUSCLE DIFFERENTIATION IN GENITAL TRACT DISORDERS.

Scully RE
Boston, MA
Arch Pathol Lab Med; 105(10):505-507 1981

The participation of smooth muscle cells and myofibroblast in neoplastic and nonneoplastic disorders of the genital tract is described. In two cases described, smooth muscle was associated with unusual lesions of the female pelvis: an endometrial cyst enveloped by a thick layer of smooth muscle in such a way that it resembled a uterus and endometriosis of a pelvic lymph node associated with smooth-muscle cells, simulating less perfectly the structure of the uterus. Nonneoplastic and neoplastic abnormalities of native smooth muscle cells have been reported in many parts of the female genital tract. Endometrial tumors that contain larger components of smooth muscle include adenomyomas confined to the endometrium, as well as adenoacanthomyomas. Pure leiomyomas occasionally arise within the endometrium. The participation of smooth muscle in nonneoplastic lesions of endometrial stroma is considered. The origin of myometrial tumors with smooth muscle elements is discussed. Smooth muscle participation in tumors of the ovary, peritoneum, and pelvic and para-aortic nodes is considered. (31 Refs)

35. CIS-PLATINUM IN GYNECOLOGIC CANCER. III. TOXICITY.

Hall DJ, Diasio R, Goplerud DR
Dept. Obstetrics and Gynecology, Univ. Tennessee Coll. Medicine, 1924 Alcoa Highway, U-27, Knoxville, TN, 37920
Am J Obstet Gynecol; 141(3):309-312 1981

The toxicity of cis-dichlorodiammineplatinum was evaluated in 41 patients who were treated for squamous cell carcinoma of the cervix or epithelial carcinoma of the ovary, with a dosage schedule of 60 mg/m2 every 3 wk. Ototoxicity occurred in 33.3% of the patients serially tested, and anemia occurred in 48.8%. Leukopenia occurred in 29.9% and thrombocytopenia in 2.2% of courses administered. Nephrotoxicity was seen in 61% of patients as determined by evaluation of blood urea nitrogen and in 70.7% by serum creatinine elevation. Urine dipstick protein and 24 hr urinary protein determinations were evaluated. Suggestions are made in regard to the use of these determinations as a guide to modification of dose and duration of therapy. (Author abstract) (21 Refs)

SELECTED PRE-CLINICAL STUDIES

36. GONADOTROPIC HORMONE BINDING TO HUMAN OVARIAN TUMORS.

Kammerman S, Demopoulos RI, Raphael C, Ross J
Dept. Medicine, New York Univ. Medical Center, 550 First Ave., New York, NY, 100 16
Hum Pathol; 12(10):886-890 1981

A variety of normal human ovarian tissues as well as benign and malignant human ovarian neoplasms have been examined in vitro for the presence of gonadotropin binding sites and gonadotropin-stimulable cAMP production, in order to determine whether gonadotropic hormones have an effect on ovarian tumors. Binding of either FSH or hCG, or both, was demonstrated in several tumors from each of the histologic subgroups of primary ovarian tumors, including epithelial, sex cord-stromal, and germ cell types. Cyclic AMP stimulation was found in one tumor of sex cord-stromal origin, in two of epithelial origin, in two of germ cell origin, and in one tumor-like condition, pregnancy luteoma. Additional biochemical studies are needed to characterize receptor sites and to relate them to histologic features, growth behavior in vivo, and serum gonadotropin levels. (Author abstract) (15 Refs)

37. DEVELOPMENT OF EXPERIMENTAL TUMORS IN THE OVARY OF A RAT AFTER TRANSPLANTATION INTO SPLEEN.

Yakushiji M, Imamura M, Masumoto R, Kato T
Dept. Obstetrics and Gynecology, Kurume Univ. Sch. Medicine, Kurume 830, Japan
Kurume Med J; 28(1):45-52 1981

Intrasplenic ovarian transplantation was performed in 222 female Wistar rats in order to observe morphological changes of the transplanted ovary over time and to study the influence of gonadotropin on tumor development. Of the 222 rats, 50 were treated with 50 IU of human chorionic gonadotropin (HCG) 3x/wk, 64 with 50 IU of PMS 3x/wk, 50 with both HCG and PMS, 34 were subjected to bilateral oophorectomy, and 4 were used as controls. No tumors developed until 25 wk after transplantation. After the 30th wk, tumors were seen in 78.8% of the transplantation group, 100% of the HCG-PMS

group, 96.1% in the PMS group, and 100% of the HCG group. Tumors included theca cell tumors, theca-granulosa cell tumors, and granulosa-theca cell tumors. After wk 30, many of the transplanted ovarian grafts were enlarged and appeared grossly as tumors. After transplantation, the wt of the ovaries increased in all groups with the greatest increase in the PMS-only group. Follicle stimulating hormone (FSH) increased after castration, reached a peak after 2-4 wk, and remained high, while luteinizing hormone (LH) increased reaching a peak at 5 wk and remained higher than controls. In the tumor-producing groups, FSH decreased but LH did not change significantly. The results indicate that gonadotropin contributes to tumor production and that FSH also plays an important role. (17 Refs)

38. INDUCTION OF UTERINE CANCER WITH INACTIVATED HERPES SIMPLEX VIRUS, TYPES 1 AND 2.

Wentz WB, Reagan JW, Heggie AD, Fu YS, Anthony DD
Reproductive Biology, Case Western Reserve Univ. Sch. Medicine, Cleveland, OH, 44106
Cancer; 48(8):1783-1790 1981

A series of studies were performed to evaluate the oncogenic potential of inactivated herpes simplex viruses Types 1 (HSV-1) and 2 (HSV-2) in the mouse cervix. HSV-1 or HSV-2 prepared in HEp-2 cells cultured and inactivated by exposure to formalin or UV light was applied to the mouse cervix for periods ranging from 20 to 90 wk. Control mice were exposed for the same period to control fluids. Vaginal cytologic preparations from all animals were examined weekly to detect epithelial abnormalities. Animals were sacrificed and histopathological studies were carried out when cellular changes seen on vaginal smears resembled those indicative of premalignant or malignant changes as previously established in a similar model system using coal tar hydrocarbons. Other animals were exposed for periods up to 90 wk, or until there was cellular evidence of invasive cancer. Cytologic and histologic materials were coded and evaluated without knowledge of whether they were from virus-exposed or control animals. Premalignant and malignant cervical lesions similar to those that occur in women were encountered in 78 to 90% of the virus-exposed animals. All controls were normal. Invasive cancer were detected in 24 to 60% of the animals and dysplasia was found in 18 to 66%. The yield of invasive cancer was twice as great after exposure to UV-inactivated HSV-2 as compared with formalin-inactivated virus. Various histologic grades of carcinoma of the cervix and endometrium were found. No primary lesions were found in the vagina or ovaries. (Author abstract) (10 Refs)

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VULVAR TUMORS

1. SEXUAL REHABILITATION OF PATIENTS WITH VULVAR CANCER.

Huffman JW
Northwestern Memorial Hosp., Chicago, IL
Med Aspects Hum Sex; 15(9):87-88 1981

While the amount of sexual rehabilitation needed by women with vulvar cancer depends on a number of factors, two problems in the lives of both pre- and postmenopausal women are psychologic disturbances and dyspareunia, which are discussed in some detail. Sexual needs should be discussed before treatment. After diagnosis and surgical treatment has been decided upon, a conference should be arranged between patient and sexual partner. (no Refs)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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CERVICAL AND UTERINE TUMORS

2. PROSPECTIVE COMPARISON BETWEEN CLINICAL AND CT STAGING IN PRIMARY CERVICAL CARCINOMA.

Walsh JW, Goplerud DR
Dept. Diagnostic Radiology, Virginia Commonwealth Univ/Medical Coll. Virginia, B ox 615 MCV Station, Richmond, VA, 23298
AJR; 137(5):997-1003 1981

For 32 mo, clinical and computed tomographic (CT) staging were compared prospectively in 75 patients with primary untreated cervix carcinoma. Clinical stages evaluated were IA (1 patient), IB (9), IIA (5), IIB (18), IIIB (38), IVA (1), and IVB (3). CT agreed with clinical stage in 65%, upstaged tumors in 19%, and downstaged tumors in 16%. In comparison with surgical stage in 25 patients, CT was inaccurate in differentiating IB and IIB lesions but highly accurate in diagnosing IIIB, IVA, and IVB tumors. Pretreatment CT was most valuable in assessing parametrial and sidewall tumor extension, uterine size, endometrial tumor extension, pelvic adenopathy, and adnexal masses. Posttreatment CT in 15 patients was most valuable in assessing extrapelvic metastases to liver, paraaortic lymph nodes, and bowel mesentery. CT offers distinct advantages over current radiologic staging techniques and can be integrated into the present International Federation of Gynecology and Obstetrics classification of cervix carcinoma. (Author abstract) (22 Refs)

3. ADOLESCENTS WITH ABNORMAL CERVICAL CYTOLOGY.

Schydlower M, Greenberg H, Patterson PH
Adolescent Medicine Service, Dept. Pediatrics, William Beaumont Army Medical Center, El Paso, TX, 79920
Clin Pediatr (Phila); 20(11):723-726 1981

Cytologic screening is an important diagnostic tool to detect precancerous and cancerous lesions of the uterine cervix. Cervical intraepithelial neoplasia (CIN) represents a continuum of neoplastic alterations, from mild dysplasia to carcinoma in situ. Our high incidence of 32/1,000 adolescent girls with abnormal cervical cytology, suggestive of CIN, supports studies showing that major cervical pathology does not exist in this age group. The importance of this problem, previous experiences, reliability of screening, management, and associated risk factors are reviewed. We advocate that the sexually active older adolescent, 18 of 21, have PAP smears at least yearly. It is also our feeling that sexually active adolescents under 18 should have annual PAP smears, even though our studies revealed a paucity of significantly abnormal findings in this age group. (Author abstract) (25 Refs)

4. OPTIMISING THE APPROACH TO CERVICAL SCREENING IN CANADA (MEETING ABSTRACT).

Shun-Zhang Y, Miller AB, Sherman G
University of Toronto, Toronto, Ontario, Canada
5th Annual Meeting of the American Society of Preventive Oncology, March 26-27, 1981, Bethesda, Maryland The Society; 1981

Using a computer simulation model of screening developed by Knox and input parameters on the natural history of the preclinical precursors of cancer of the cervix from a cohort study of women in British Columbia from 1949-69, an attempt has been made to evaluate different approaches to screening using the pap smear. The natural history input parameters and the output parameters without screening were modified to reflect the earlier onset of carcinoma in situ in younger cohorts than those studied in British Columbia resulting in a mortality from cancer of the cervix approx 50% greater than operated in the referent yr. It has been found that the sensitivity of the test and the proportion of women in the population who accept invitations to attend for screening materially influence the extent to which programs reduce mortality. Thus a reduction in the proportion attending from 80% to 50% produces a far greater impact than variation in age of onset of screening, frequency of rescreening or age of cessation of screening. Missed screens also have an important impact. On the basis of these simulations, an optimal program might commence at age 25, involve three yearly screens to age 40 and five yearly to age 60, a total of ten tests in a life-time. A repeat test at age 26 contributes nothing to the mortality benefit. Such a schedule, using a test of 75% sensitivity with 80% population acceptance, would reduce lifetime mortality from cancer of the cervix by at least 90%. (no Refs)

5. SCREENING OF ASYMPTOMATIC WOMEN FOR ENDOMETRIAL CANCER.

Koss LG, Screiber K, Oberlander SG, Moukhtar M, Levine HS, Moussouris HF
Dept. Pathology, Albert Einstein Coll. Medicine, Montefiore Hosp. Medical Center, Bronx, NY
CA; 31(5):300-317 1981

This report describes the preliminary results of a feasibility study of detection of endometrial carcinoma in an asymptomatic population of women aged 45 and above. The initial sample of 1,280 women was evaluated by several cytologic smear techniques and by two endometrial sampling methods assigned by computer. The clinical approaches and the techniques used are detailed. During this initial period of study, eight histologically proved endometrial cancers were diagnosed, two of which were deeply invasive. With one exception, the eight patients were either obese or had a history of treatment with conjugated estrogens. A relatively small number of women with endometrial hyperplasia of various types were also identified. The accuracy of the detection methods and their long-term impact on morbidity and mortality cannot be assessed as yet. Incidentally, a small number of cancers and precancerous states of organs other than the endometrium have also been diagnosed. (Author abstract) (31 Refs)

6. PROGNOSTIC VALUE OF CYTOLOGIC EXAMINATION OF PERITONEAL WASHINGS IN PATIENTS WITH ENDOMETRIAL CARCINOMA (MEETING ABSTRACT).

Szpak C, Creasman W, Vollmer RT, Johnston WW
Duke University Medical Center, Durham, NC
Acta Cytol (Baltimore); 25(4):447 1981

Peritoneal pelvic washings from 23 women with endometrial carcinoma were evaluated in a blind retrospective fashion for the concentration of malignant cells present on two membrane filters. In 19 women, the pelvic washings were obtained at the time of primary surgical extirpation, while in 4 they were obtained during exploratory laparotomy for suspected recurrent carcinoma. None of the six patients with pathologic stage I disease and negative washings developed recurrence after follow-up of 16 to 45 mo. Four of nine patients with pathologic stage I disease and an excessive concentration or malignant cells in the washings died as a consequence of carcinoma within two yr. The remaining five patients with pathologic stage I disease and a reduced concentration of malignant cells in the washings had no evidence of disease for 33 to 51 mo, resembling those

patients with negative washings. A mathematical model (Cox's nonparametric statistical analysis) was used to relate the concentration of malignant cells in washings to survival. Thus, examination of pelvic washings at the time of primary operative treatment or of exploratory laparctomy has predictive utility for likelihood of recurrence. The abundance of malignant cells has prognostic importance in identifying those patients with pathologic stage I disease who may require more aggressive therapy in the absence of histologic involvement. (no Refs)

7. FALLOPIAN TUBE AND PELVIC CYTOLOGY IN ENDOMETRIAL CARCINOMA (MEETING ABSTRACT).

Kulcher LK, Marshall RB, Breedin PH, Homesley HD
Department of Pathology, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, NC
Acta Cytol (Baltimore); 25(4):436 1981

The study of peritoneal washing cytology is an intergral part of staging and treatment of endometrial carcinoma. In 30 patients with FIGO clinical stage 1A, 1B or occult II endometrial carcinoma, cytology was positive or suspicious in three patients with negative lymphadenectomy and in one patient with a positive lymph node. The following procedure was developed to define the possible role of malignant cells exfoliated through the fallopian tubes as a mechanism for recurrence of intrauterine endometrial carcinoma with negative lymphadenectomy. A pelvic washing (100 ml normal saline) was collected on entering the pelvis for filter and cell block study. The fallopian tubes were then clamped at the isthmus, resected and sent to pathology. The surgeon proceeded with the treatment and staging operation. The clamp was removed and the fimbriated end cannulated with a 16-gauge angiocath. Each tube was washed with 25 ml of normal saline and collected for filter preparations. Cytologic diagnoses by three independent reviewers were then correlated with histologic findings. Cases with direct involvement of fallopian tube or advanced histologic stage were excluded. Three of 12 initial patients had positive tubal cytology, while 1 of the 3 had positiv e pelvic cytology. The value of this procedure to explain in part the 12% recurrence rate noted in adenocarcinoma localized in the uterus and its clinical applications are under continuing study. (no Refs)

8. DISCOVERY RATE OF DYSPLASIA AND CARCINOMA OF UTERINE CERVIX IN AN URBAN MEDICAL CENTER AND CLINICS, NEWARK, N.J. FROM 1972 TO 1978 (MEETING ABSTRACT).

Riccio JA, Chou J, Chung HR
New Jersey Medical School, Newark, NJ
Twenty-ninth Annual Scientific Meeting of the American Society of Cytology, November 2-7, 1981, St. Louis, Missouri. The Society 90 pp., 1981.

File analysis on 98,970 cases with the aid of a computer was performed. Cytologic evaluation was done at the New Jersey Medical School. Most of the data was put into the computer using the cytology laboratory file and these data were evaluated. The material was collected from January 1, 1972 to December 31, 1978 consisting of 98,970 cytologic specimens from 58,053 patients. Total atypical cases without repeat were 1537 including 985 cases of mild to moderate dysplasia, 326 cases of moderate to severe dysplasia, 136 cases of carcinoma in situ, and 90 cases of invasive carcinoma. Cases of glandular atypia and adenocarcinoma were excluded from this study. The peak values for age specific discovery rates of dysplasia was found in the 25-29 age group, for carcinoma in situ 40-44 yr of age, and for invasive carcinoma 50-54 yr of age. The mean age of mild to moderate dysplasia is 25.6 yr, moderate to severe dysplasia 29.3 yr, carcinoma in situ (CIS) 33.3 yr and invasive carcinoma 52.3 yr of age. Approx 75% of mild to moderate dysplasia, and 64% of moderate to severe dysplasia were between the ages of 15 and 29 yr of age. Significant numbers of dysplasia seem to manifest at the ages under 15 yr. Shifting of mean ages of precancerous conditions and carcinoma in situ to much earlier ages and concentration of dysplasia and at the younger age group could raise the possibility that all these trends represent not only regional, but possibly national trends. The above findings and also a significant rate of dysplasia in the ages under 15 yr may indicate that the 'Pap' test should be instituted at a much earlier age. (no Refs)

9. TUBAL (SEROUS) CARCINOMA OF THE ENDOMETRIUM.

Lauchlan SC
Dept. Pathology, Women and Infants Hosp. Rhode Island, 50 Maude St., Providence, RI, 02908
Arch Pathol Lab Med; 105(11):615-618 1981

The logic of cancer histopathology demands that the presence of tubal epithelium in the endometrium be followed in some cases by the corresponding carcinoma. With tubal epithelium, this carcinoma is the homologue of the serous carcinomas of the ovary or the usually encountered carcinoma of the oviduct. A series of eight of these cases was studied. Many of the features were similar to those of ordina ry endometrial carcinoma, but the prognosis was strikingly worse; many of the patients died of widespread metastases, with no or only minimal myometrial invasion. (Author abstract) (9 Refs)

10. ADENOMATOID TUMORS OF THE UTERUS.

Quigley JC, Hart WR
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Am J Clin Pathol; 76(5):627-635 1981

Adenomatoid tumors arising in the uterus are not well-recognized and are sometimes mistaken for other benign or malignant neoplasms. This study is a clinicopathologic analysis of 12 uterine adenomatoid tumors. Characteristically, they were small nodular lesions (mean diameter 2.1 cm) in the subserosa or outer wall of the myometrium. Four distinctive histologic types (adenoid, angiomatoid, solid, and cystic) were identified; each tumor consisted of a combination of one major and at least one minor type. The nodular proliferation of smooth muscle which accompanied some tumors was regarded as a non-neoplastic hyperplasia of myometrium. In two cases, small foci of serosal endosalpingosis were adjacent to the tumor. Theories of histogenesis are discussed, and classification of the adenomatoid tumor as a type of benign mesothelioma is endorsed. (Author abstract) (30 Refs)

11. CEA, AFP, FSH, LH, HCG-B AND PRL VALUES IN THE SERUM OF UTERINE CERVICAL CANCER PATIENTS (MEETING ABSTRACT).

Hsu CT, Hsu TH, Chen WH
Department of Obstetrics and Gynaecology, Taipei Medical College, Taipei, China
Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.

One hundred and four out of 224 (46.43%) uterine cervical cancer patients showed elevated carcinoembryonic antigen (CEA), 31 out of 222 (13.96% patients elevated luteinizing hor-

mone (LH), 23 out of 220 (10.45%) patients elevated follicle stimulating hormone (FSH), 78 out of 216 (36.11%) patients elevated prolactin, 6 out of 216 (2.78%) patients elevated alpha-fetoprotein (AFP) and 15 out of 224 (6.70%) patients elevated human chorionic gonadotropin (hCG-b). Only CEA showed a correlation with the size of the primary tumor, and stage of the disease, and also possessed a clinical significance in detection of recurrence. High hCG-b values seems to be somewhat related to poor prognosis. A high PRL value also is of some clinical significance, however, not definite. AFP, FSH and LH seem less significant in prognostication. These findings will be illustrated with some particular cases. (no Refs)

12. T CELL SUBSETS (T GAMMA, T MU) AND T CELL MEDIATED SUPPRESSOR OR HELPER FUNCTION IN PATIENTS WITH CERVICAL CANCER (MEETING ABSTRACT).

Shiraki S, Mori H, Kadomoto N, Yamada Y, Hayasaki M, Noda K
Department of Obstetrics and Gynaecology, Gifu University, Gifu, Japan
Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.

In 54 patients with cervical cancer, T cell subsets (T gamma, T mu) were detected with new simple methods. Helper and suppressor function of T cell were examined in a pokeweed mitogen induced B cell differentiation system. The enhancement effect of helper activity of T cells was also examined with functional abrogation technique of suppressor T cells by Mitomycin C treatment. T gamma proportion increases progressively as the tumor grows. In patients with regional lymph node metastasis, the T gamma proportion significantly increased (28.9%). The T mu proportion was about 40% in stage I-III. After surgical removal of tumor, the T gamma proportion fell rapidly to the normal range, whereas a tendency to increase gradually was shown in the T mu proportion. In most patients who showed elevated suppressor and depressed helper function, improvement of these functions was observed at 4 wk after operation. Mitomycin C treatment-induced enhancement was less than 2.5-fold in normal persons; by contrast, it was more than 2.5 and fold in patients (8/15 cases), therefore seemed to be an activation of suppressor T cells in these patients. The findings suggest that these changes of T cell subsets may reflect the presence and progress of tumor and that the immune suppression in cancer patients is a complex constellation of abnormalities of numbers and/or function of helper and suppressor cells. (no Refs)

13. CRYOTHERAPY IN CERVICAL DISEASE.

Sedlis A, Castadot MJ, Glatt B
Dept. Obstetrics and Gynecology, State Univ. New York, Downstate Medical Center, 450 Clarkson Ave., Brooklyn, NY, 11203
NY State J Med; 81(12):1757-1760 1981

Two hundred and 21 women with CIN-1 and CIN-2 (mild or moderate cervical intraepithelial dysplasia) proved on colposcopic biopsy and 317 women with benign cervical disease were treated by cryotherapy. Of these, 178 CIN patients were followed from 6 to 80 mo and monitored for residual disease with Papanicolaou smears and colposcopic biopsies; 43 patients were lost to follow-up. In 18 patients (10.1%) residual CIN-1, CIN-2, or progression to CIN-3 (severe dysplasia) was diagnosed from 6 to 50 mo after cryotherapy; in 7 of these patients (39%), the diagnosis was made 18 or more mo after treatment. Twelve patients with persistent CIN-1 or CIN-2 received second cryotherapy after which progression occurred in 2 patients and persistent disease was found in 3. Six patients showed no residual CIN. CIN-1 or CIN-2 was diagnosed in 4 out of 181 women treated with cryotherapy for benign cervical disease. All patients treated with cryotherapy for cervical neoplasia must be closely monitored for long periods of time because the residual disease occurs in over 10% of cases and may not be recognized for many mo or yr. (Author abstract) (20 Refs)

14. A PHASE I STUDY OF MISONIDAZOLE AND PELVIC IRRADIATION IN PATIENTS WITH CARCINOMA OF CERVIX (MEETING ABSTRACT).

Thomas GM, Rauth AM, Black BE, Cummings BJ, Sorrenti VL, Bush RS
The Ontario Cancer Institute, Toronto, Ontario, Canada
Conference on Chemical Modification: Radiation and Cytotoxic Drugs, September 17-20, 1981, Key Biscayne, Florida. Committee for Radiation Oncology Studies 139 pp., 1981.

A dose seeking Phase I study of oral misonidazole administered daily with conventional pelvic irradiation has been conducted in patients with carcinoma of the cervix Stages, IB, IIB, IIIB and IVA. Pharmacological parameters, measured for blood and urine specimens using high pressure liquid chromatography, were examined for correlation with clinically observed toxicities. Misonidazole was administered in escalating daily dosage levels to sequential groups of patients at doses of 0.15 g/M2, 0.30 g/M2 or 0.45 g/M2 for 22 days over five wk. Sixteen patients were assigned to each dose level. Using a double blind randomization they received either placebo (3/16) or misonidazole (13/16). The lowest dose level was completed and evaluated before progressing to the next level. The major dose limiting toxicity observed was peripheral neuropathy (PN). None of the 13 patients at the 0.15 g/M2 level, and 0/13 at the 0.3 g/M2 level developed PN. However, 6/13 at the 0.45 g/M2 developed mild to moderate PN. Additional patients were entered at this level and at present 8/17 have developed PN. The onset of all neuropathies occurred between the 12th day of taking drug to 10 days after drug ceased and were maximal within one wk of onset. Symptoms of PN have persisted for durations between 1 and 11 mo and to date have been completely reversible in only 3/8 patients, however in those with PN of duration greater than or equal to 3 mo significant improvement has occurred. Detailed plasma kinetics were measured on the 1st and 20th day of drug treatment. Although peak plasma misonidazole levels and half-lives of the first drug dose did not predict for development of PN, the calculated 'area under the curve' (AUC) correlated strongly with development of PN. The range of AUC's for these patients was 804 uM-hr to 2050 uM-hr. All but one patient developing PN and a AUC greater than 1000 uM-hr. To date no correlation exists between PN and total urinary excretion of misonidazole, levels of o-demethylation product or the amine of misonidazole in urine. (no Refs)

15. THE ROLE OF ADJUNCTIVE RADIOTHERAPY FOR STAGE I ENDOMETRIAL CARCINOMA: PREOPERATIVE VS POSTOPERATIVE IRRADIATION.

Chung CK, Stryker JA, Nahhas WA, Mortel R
Div. Radiation Oncology, Milton S. Hershey Medical Center, Hershey, PA
Int J Radiat Oncol Biol Phys; 7(10):1429-1435 1981

Eighty-five consecutive unselected patients with Stage I endometrial carcinoma (adenocarcinoma, 75; adenoacanthoma 6, adenosquamous carcinoma 4) underwent treatment with surgery alone (13), preoperative (preop) radiotherapy (RT) and subsequent surgery (33), surgery plus postoperative (postop)

RT (36) or RT alone (3). Surgery consisted of abdominal hysterectomy and bilateral salpingo-oophorectomy. Preop RT was given 4-6 wk prior to, postop RT 2-4 wk following surgery. Deep myometrial invasion (outer one-third of thickness) was 6% and 28% in the preop and postop RT groups, respectively. Eleven patients developed recurrences, two in the vagina only, four in the pelvis and distant metastases, and five distant metastases only. Recurrences occurred within 24 mo in 81% and within 48 mo for all patients. Distant metastasis only developed in Stage IB patients (lung 3, diffuse peritoneal cavity 3, liver 2, pleura 1). Five yr survival rates were surgery only 63%, preop RT 88%, postop RT 90. Two of the three RT only cases survived 2 yr. It is noted that postop RT offers the advantage of accurate surgical and pathological staging and optimal adjustment of therapy. Those with deep myometrial invasion and/or Grade 3 tumors may require systemic therapy because of the high incidence of distant failures. (27 Refs)

16. A MICROWAVE APPLICATOR FOR INTRACAVITARY HYPERTHERMIA OF CARCINOMA OF THE CERVIX (MEETING ABSTRACT).

Hand JW, Blake PR, Hopewell JW, Lambert HE, Field SB
MRC Cyclotron Unit, Hammersmith Hospital, Ducane Road, London W12 OHS, England
Strahlentherapie; 157(9):618 1981

Incidence of carcinoma of the cervix is increasing. Since more early-stage disease is seen now than in the past, the failure of local control is a frequent problem despite improvements in the accuracy of staging and radiotherapy planning. Hyperthermia may prove to be a useful treatment since squamous cervical tumors are thought to contain a high proportion of hypoxic cells. In early clinical studies, favorable responses have been observed in tumors treated by hyperthermia in combination with radiotherapy. We have designed microwave applicators which are compatible with the standard plastic after loading tubes used with linear cesium sources for conventional intracavitary treatment. The applicators operate at frequencies in the range of 800-1000 MHz and use a dielectric encapsulated dipole as the radiating element. In clinical use, the microwave heater will be inserted into the afterloading tube, without subjecting the patient to further trauma, approx four hr after intracavitary radiotherapy. These applicators are described, and a preclinical assessment of them, as measured in phantom materials and pigs, is discussed. (no Refs)

17. TAMOXIFEN IN ADVANCED ENDOMETRIAL CANCERS RESISTANT TO PROGESTAGENS (MEETING ABS TRACT).

La Vecchia C, Franceschi S, Colombo E, Mangioni C
Mario Negri Institute for Pharmacological Research, Milan, Italy
Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

Endometrial cancers never sensitive to or resistant to progestational therapy have recently been reported as showing some response to antiestrogens. Seventeen patients with advanced endometrial cancer were treated from May 1978 to December 1980 with Tamoxifen citrate (20 mg/day po) for at least 3 mo after failure with high dose progestins (medroxyprogesterone acetate (MPA) 1000 mg/day po for at least 3 mo). Age ranged from 60 to 81 yr (median 69); 8 patients had pelvic, 3 abdominal metastases, 6 distant dissmemination (4 lung metastases). Fifteen patients were evaluable. Five patients had no change; 4 are alive after 5, 9, 10 and 11 mo, the 5th died of tumor after 5 mo. Ten patients had progression; 2 are alive after 3 and 6 mo, 8 died of tumor after 3 to 14 mo. These data do not confirm the previous indication of the efficacy of Tamoxifen in patients resistant to progesterone. A possible explanation of this discrepancy is that the patients in this study had been treated extensively with high-dose MPA. (no Refs)

18. MEDROXYPROGESTERONE ACETATE (MPA) IN ADVANCED CERVICAL CANCER (MEETING ABSTRACT).

Mangioni C, La Vecchia C, Franceschi S
1st Obstetrics and Gynecology Clinic, University of Milan, Milan, Italy
Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

Between July 1978 and December 1979, 34 patients (pts) aged from 34 to 74 yr (median 56) with advanced cervical cancer were allocated at random to one of two MPA regimens: 1) 800 mg daily po for at least 12 wk (18 pts); 2) 500 mg daily im for the first 4 wk; 500 mg twice weekly for the second 4 wk; 500 mg once weekly for the next 4 or more wk (16 pts). Thirty-two patients were evaluable; 30 had been previously treated with external pelvic radiotherapy; 19 had received at least one chemotherapy regimen. No objective response or stable disease was obtained among 26 epidermoid carcinomas; 2 patients experienced subjective improvement. Two out of six adenocarcinomas had stable disease lasting 7 and 12 mo; 3/6 had subjective improvement. Treatment was well tolerated by both routes of administration. (no Refs)

19. PROGESTERONE RECEPTORS AS AN INDICATOR OF THE RESPONSE OF POST-MENOPAUSAL ENDOMETRIAL CARCINOMA AND METASTATIC BREAST CANCER TO AN ANTIESTROGEN (MEETING ABSTRACT).

Robel P, Mortel R, Levy C, Namer M, Baulieu EE
Laboratory Hormones, 94270 Bicetre, France
Progesterone and Progestins, International Symposium, May 7-9, 1981, Paris, France Centre National de la Recherche Scientifique; 1981

Estradiol (ER) and progesterone receptor (PR) concentrations were determined in cytoplasmic and nuclear fractions of endometrial cancer specimens taken from 43 post-menopausal women. All tumors except 1 contained variable, often large, amounts of total ER. The total PR concentration was generally low and considered undetectable or insignificant in 10 cases. No significant correlation was found between receptor concentrations and histological grading. Fifteen patients received tamoxifen (Tam) po (40 mg daily for 5 to 7 days, Group 1) and 10 patients ingested 10 mg of Tam 8 and 4 hr prior to a second endometrial sampling (Group 2). In addition to receptors, ornithine-decarboxylase activity (ODC) was also measured before and after Tam treatment. PR concentrations in Group 1 increased significantly but ODC did not. Because Tam may have induced a rapid and transitory increase of enzyme activity, ODC was studied in Group 2 patients. Again no change in the enzyme activity was observed. PR did not vary but nuclear ER increased indicating Tam effectiveness. Available cytoplasmic ER and PR sites were measured in biopsies of skin metastatic nodules removed from 21 post-menopausal women with advanced breast cancer. All patients received 30 mg of Tam daily for 7 days. When present, ER was greatly decreased. No PR change was recorded in cases where ER was less than 20 fmol/mg cytosol protein. Six of the 12 remaining cases showed an increase of PR greater than 100 fmol/mg cytosol protein. We conclude that repeated tumor sampling should be consid-

ered whenever possible, allowing an in vivo challenge with Tam to predict hormone responsiveness on the basis of large PR increase. (no Refs)

20. CYTOPLASMIC PROGESTERONE AND ESTRADIOL RECEPTORS IN NORMAL, HYPERPLASTIC, AND CARCINOMATOUS ENDOMETRIA: THERAPEUTIC IMPLICATIONS.

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Am J Obstet Gynecol; 141(5):539-546 1981

This study was designed to determine whether the presence of progesterone receptors (PR) and/or estradiol receptors (ER) could be used to predict progestin responsiveness of recurrent or advanced endometrial cancers. We have demonstrated the presence of physicochemically similar cytoplasmic progesterone and estradiol receptors in normal, hyperplastic, and carcinomatous endometria. All normal endometria contained both PR and ER. Seventy-three percent of endometrial hyperplasias were PR(+) and 93% were ER(+). A decreasing concentration of progesterone receptor activity was observed with increasing tumor anaplasia [Grade 1, 84% PR(+); Grade 2, 55% PR(+); Grade 3, 22% PR(+)] and in irradiated tumors. A statistically significant (p less than 0.001) relationship has been demonstrated between the presence of specific cytoplasmic PR and response to progestin therapy in recurrent or advanced endometrial adenocarcinomas. Thus, we conclude that a PR assay may be used to help select the most appropriate therapy for patients with recurrent or advanced endometrial adenocarcinoma. (Author abstract) (42 Refs)

21. CYTOSOL ESTROGEN AND PROGESTIN RECEPTORS IN ENDOMETRIAL CARCINOMA: CLINICAL CORRELATES (MEETING ABSTRACT).

Kauppila A, Kujansuu E, Vihko R

University of Oulu, Oulu, Finland

Progesterone and Progestins, International Symposium, May 7-9, 1981, Paris, France Centre National de la Recherche Scientifique; 1981

Cytosol progestin (PR) and estrogen receptor (ER) concentrations in 114 endometrial carcinoma samples from 109 patients were correlated with clinical and histopathological characteristics and clinical outcome of 44 patients followed-up for at least 2 yr after the primary therapy. Eighty percent of all samples were simultaneously PR- and ER-positive whereas 10% were receptor-negative. Receptor-negative tumors behaved more aggressively both in early and advanced clinical stages than did receptor-positive tumors. Early clinical stages (I and II) were often receptor positive and the receptor concentrations in these tumors were higher than in advanced or recurrent diseases or in anaplastic tumors. On the other hand, PR and ER concentrations did not correlate with the patient age or menopausal status, body wt or carbohydrate metabolism. PR and ER determinations seem to serve as practical aids in the selection of appropriate chemotherapy in advance endometrial cancer, as recorded previously; and based on the present data, as prognostic risk factors which might be useful in selection of the most efficient treatment modalities in individual patients. (no Refs)

22. PROGESTERONE RECEPTORS IN ENDOMETRIAL CARCINOMA (MEETING ABSTRACT).

Pollow K, Grill HJ, Manz B

Johannes Gutenberg University, Mainz, Germany

Progesterone and Progestins, International Symposium, May 7-9, 1981, Paris, France Centre National de la Recherche Scientifique; 1981

The following investigation was undertaken in an attempt to present a comparison of biochemical and physical properties as well as the quantity of progesterone receptors (PR) in normal and neoplastic endometrium. Using the dextran-coated charcoal assay, we could demonstrate that progesterone receptor levels in cytosol of normal endometrium are directly dependent on the stage of the menstrual cycle, with a max in the late proliferative phase and a sharp decrease during the second half of the menstrual cycle. The receptor levels in the cytosols of endometrial carcinomas were correlated with histological type of the tumor. The level of progesterone binding sites was highest in well-differentiated tumors. Thirty-six of our recurrent endometrial carcinomas have been evaluated for their response to gestagen therapy after having progesterone receptor activity measured. All PR+ endometrial carcinomas responded to gestagen therapy while only 5 out of 22 PR- endometrial carcinomas responded. When tissue samples were taken from patients before and after administration of ethinyl-estradiol the mean PR levels in the well-differentiated and to a lesser extent in the moderately well-differentiated endometrial carcinomas were markedly increased, demonstrating that the hormonal stimulus leads to similar effects as in normal endometrium. Medroxy progesterone acetate-treatment leads to a decrease in PR content of tumor samples, which were collected from the same patient before and after a two to four wk treatment with medroxy progesterone acetate. These findings indicate that the neoplastic tissue may contain a progestin receptor similar or identical to the one from normal endometrial cytosol. (no Refs)

23. CLEAR CELL CARCINOMA OF THE ENDOMETRIUM: AN UNCOMMON ENTITY WITH A FAVORABLE PROGNOSIS.

Shankar PG, Schneider V, Belgrad R

Dept. Radiation Oncology, St. Louis Univ. Hosp., 325 S. Grand Blvd., St. Louis, MO, 63104

Int J Radiat Oncol Biol Phys; 7(10):1383-1387 1981

Experiences with 23 cases of clear cell carcinoma (CCCM) among 345 patients with endometrial carcinoma seen between 1969 and 1978 are presented. Earlier series indicate that patients with CCCM have a worse prognosis compared with classical endometrial adenocarcinoma. The series of 23 cases showed no differences compared to classical adenocarcinoma with regard to age, race, stage at presentation or response to treatment. It is concluded that while CCCM is a definite histological entity, it does not behave any differently than classical adenoma in its presentation or response to treatment. Appropriate treatment for CCCM is a combination of surgery and radiotherapy. (14 Refs)

24. AN ANALYSIS OF DETECTION BIAS AND PROPOSED CORRECTIONS IN THE STUDY OF ESTROGENS AND ENDOMETRIAL CANCER.

Greenland S, Neutra R
Div. Epidemiology, Sch. Public Health, Univ. California, Los Angeles, CA, 90024
J Chronic Dis; 34(9/10):433-438 1981

We present an algebraic analysis of detection bias and the Horwitz-Feinstein correction in the study of estrogens and endometrial cancer. This analysis sets forth precisely how the validity of conventional study results depends on the cancer detection rates, and how the validity of the Horwitz-Feinstein 'alternative' approach depends on both the detection rates and the rates of the medical intervention employed as the matching factor. Numerical examples demonstrate that the observed results of both conventional and alternative studies are mutually compatible with a broad range of true values of the association under study, and that there is no a priori basis for assuming that either set of results is closer to the true value. Nevertheless, estimates of exposure-specific disease detection rates can be used to evaluate the extent of bias present in conventional results. (Author abstract) (9 Refs)

25. EXOGENOUS ESTROGENS AND ENDOMETRIAL CANCER: A CASE-CONTROL STUDY AND ASSESSMENT OF POTENTIAL BIASES.

Spengler RF, Clarke EA, Woolever CA, Newman AM, Osborn RW
Dept. Preventive Medicine and Biostatistics, Univ. Toronto, Ontario, M5S 1A8, Canada
Am J Epidemiol; 114(4):497-506 1981

Eighty-eight cases with newly diagnosed carcinoma of the endometrium and 177 age-matched neighborhood controls were interviewed to test the hypothesis that exogenous estrogens lead to an increased risk of endometrial cancer. Forty-five percent of the cases and 22% of the controls reported a history of estrogen use which yielded an odds ratio of 2.9 (confidence interval (CI) 1.7-5.1). Women with 5 or more yr of estrogen use had an odds ratio of 8.6 (CI 3.2-23.0). Approx 80% of the estrogen users had used conjugated equine estrogens. For these women the odds ratio was 4.0 (CI 1.9-8.4) for daily dosages of more than 1 mg of estrogen. Several sources of bias which might affect the estrogen association were investigated. These included comparability of cases and controls, selection procedures, difference between estrogen users and nonusers, exclusion of controls who had hysterectomy, source of estrogen information, and differential recall. The concept of medical surveillance was evaluated by access to medical care and prior history of dilatation and curettage. The strong association between exogenous estrogen use and endometrial cancer remained after consideration for the effects of these biases. (Author abstract) (23 Refs)

26. A GEOGRAPHICAL STUDY OF ANTIBODIES TO MEMBRANE ANTIGENS OF HSV-2-INFECTED CELLS AND HSV-2-SPECIFIC ANTIBODIES IN PATIENTS WITH CERVICAL CANCER.

Mendis LN, Best JM, Senarath L, Chiphangwi J, Vestergaard BF, Banatvala JE
Dept. Microbiology, Faculty of Medicine, Post Office Box 271, Kynsey Road, Colombo 8, Sri Lanka
Int J Cancer; 28(5):535-542 1981

Sera were obtained from patients with squamous carcinoma of the cervix from Great Britain (29), Sri Lanka (32), Malawi (27) and Sudan (27), and from controls from all countries except Sudan. Controls were matched for ethnic origin, age and social class. Sera were tested by indirect immunofluorescence (IF) for IgG and IgA antibodies to membrane antigens (MA) and IgA antibodies to VCA of HSV-2 infected cells. Compared with controls, IgA antibodies to MA (IgA anti-MA) were detected more frequently and at higher titers in all groups of patients. However, there was no significant difference in prevalence of these antibodies at titers greater than or equal to 1:4 between Malawian patients and controls, although a significantly higher proportion of patients had IgA anti-MA titers of greater than or equal to 1:16. In contrast, IgA anti-VCA did not distinguish patients from controls. More than 90% of both patients and controls from all countries had IgG antibodies to MA (IgA anti-MA). Malawian patients had a significantly higher geometric mean titer (GMT) of IgG anti-MA than controls and both patients and controls had significantly higher GMTs than their counterparts from other countries. The variation between herpes IgG anti-MA titers in subjects from different countries did not reflect differences in serum Ig levels and similar variations in titer were not seen in rubella and measles HAI titers. Among the patients there was a geographical variation in the prevalence of HSV-2 specific antibodies detected by ELISA, which varied from 52% among British and Sudanese patients to 73% among Malawian patients. Even when adjustment was made for possible false negative results, there were between 10 and 31% patients without HSV-2-specific antibodies, although only 2 of 103 (1.9%) patients had neither HSV-1 nor HSV-2 antibodies. The association of HSV-2 with cervical carcinoma appeared to vary with age. (Author abstract) (52 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

27. ABDOMINAL ULTRASOUND IN ADVANCED OVARIAN CARCINOMA.

Paling MR, Shawker TH
Dept. Diagnostic Radiology, NIH, Clinical Center, Bldg, 10 Rm 6S211, Bethesda, MD, 20205
JCU; 9(8):435-441 1981

The ultrasonic appearance of pelvic tumor and intra-abdominal dissemination is reported in 57 patients with advanced ovarian carcinoma. The primary pelvic tumor was found to be solid or mixed solid-cystic. In no case was the primary malignancy exclusively cystic. In 23 patients, intra-abdominal extrapelvic tumor was detectable, and in 8 patients there were solid liver metastases. The usefulness of both static and real-time ultrasound scanning in detecting Stage III and IV disease is discussed. (Author abstract) (18 Refs)

28. COMPUTER-ASSISTED ULTRASOUND DIAGNOSIS OF OVARIAN TUMORS (MEETING ABSTRACT).

Sekiba K, Fukumoto S, Fujita T, Akamatsu N
No affiliation given
Excerpta Med Int Cong Ser; 547:50 1981

The diagnostic procedure for ovarian tumors has been reported by many authors, but no quantification method using the computer has been reported. This study concerns a retrospective observation of 159 ovarian tumors, histologically confirmed, during the past 5 yr. To discriminate malignant from benign we have been able to extract 6 statistically significant factors out of 16 echographic features of these tumors. The 6 selected factors are: (1) solid part with irregularity, (2) irregu-

lar wall of the cystic part, (3) septum in a cystic part, (4) irregularly shaped tumor, (5) ascites, and (6) tumor size more than 10 cm in diameter. We gave scores to each of the above parameters and then reevaluated the factors and the scores by computer using the theory of Hayashi's quantification number 2. These established criteria and formula are programmed and memorized into the mini-floppy disc for routine use. Ultrasound information in daily use is fed via keyboards into the microcomputer by TSS. The data are analyzed by microcomputer and results can be printed in real-time. (no Refs)

29. CYTOLOGIC FINDINGS OF BORDERLINE (LOW-GRADE) MALIGNANT TUMORS OF THE OVARY (MEETING ABSTRACT).

Kanbour A, Wagner J, Commisso J
University of Pittsburgh School of Medicine, Pittsburgh, PA
Acta Cytol (Baltimore); 25(4):448 1981

Eighteen patients were diagnosed as having borderline or low-grade ovarian malignancy at Magee Womens Hospital from 1974 to 1980. Five were of the mucinous and 13 of the serous variety. The patients' ages were 21 to 59 yr; five were younger than 27 yr. The tumor was in stage I in 11, stage II in 2 and stage III in 5 patients. It has been established that the borderline, or low-grade, malignant tumor of the ovary has two main parameters distinguishing if from outspoken cancer. These include the absence of invasion and a favorable prognosis. The cytologic presentations in 12 peritoneal washings and 6 peritoneal effusions were reviewed to establish cytologic criteria that may help to distinguish this particular tumor entity. No tumor cells were found in 11 cases. In the remaining seven, malignant cells were present; five of these corresponded to clinical stage III and one each to stage II and stage I. All were of the serous variety. The majority of tumor cells were observed in tissue fragments or papillary clusters. Individual tumor cells were relatively small, with a high nuclear-cytoplasmic ratio and a finely-to-coarsely-granular chromatin pattern. Prevalence of prominent micronucleoli was observed. A moderate-to-large number of psammoma bodies was present in all cytologically positive specimens. When compared to borderline lesions, tumor cells in peritoneal fluids of outspoken serous carcinoma were found to be larger, with prominent macronucleoli; not only tissue fragments but also single cells were frequent; and psammoma bodies were reported to be present in only one-third of the cases. Recognition of this tumor type in cytologic material is essential since the prognosis is favorable and less aggressive treatment is required. (no Refs)

30. SERTOLI-LEYDIG CELL TUMOR WITH RHABDOMYOSARCOMA. ULTRASTRUCTURE AND REVIEW OF LITERATURE (MEETING ABSTRACT).

Arguelles MT, Alonso NO, Martin JA, Martinez AM, Fuente EM, Ferenczy A
Department of Pathology, Residencia Sanitaria, Gijon, Spain
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

A case of moderately differentiated Sertoli-Leydig cell tumor with predominance of rhabdomyosarcoma occurring in the ovary of a young female was examined by light and electron microscopy. The Sertoli cells were found morphologically and pathogenetically distinct from rhabdomyoblasts. The latter demonstrated varying degrees of differentiation and probably originated from the uncomitted stromal fibroblasts of the ovary. According to review of the published world literature, this is the first well-documented case of Sertoli-Leydig cell tumor with rhabdomyosarcoma of the ovary. (no Refs)

31. AFP IN YOLK SAC TUMOR AND SOLID TERATOMA OF THE OVARY: SIGNIFICANCE OF POSTOPERATIVE SERUM AFP.

Ishiguro T, Yoshida Y, Tenzaki T, Ohshima M, Suzuki H
Dept. Obstetrics and Gynecology, Shiga Univ. Medical Science, Seta, Ohtsu 520-21, Japan
Cancer; 48(11):2480-2484 1981

Serial serum alpha-fetoprotein (AFP) was examined postoperatively in five patients with yolk sac tumor and in three with solid teratoma of the ovary. Serial estimation of AFP was also done in sera from postpartum patients to compare the decreasing ratio between the two groups. Serum AFP in these postpartum women decreased according to the exponential function curve as AFP = be-mx (x = days after delivery) with a mean m value of 0.1652 and a mean correlation coefficient of-0.9911. Half-time of serum AFP in postpartum subjects was 4.33 days. Exponential decrease of serum AFP was also found in postoperative patients with yolk sac tumor and solid teratoma of the ovary. However, in those in whom there was an incomplete removal of the tumors, the values of either m or coefficient of correlation were significantly lower as compared to those in patients with compiete extirpation of lesions or those in postpartum subjects. Elevation of serum AFP was noted postoperatively in two patients with recurrences; however, significant decreases in AFP following chemotherapy were apparent in one patient with immature solid teratoma. These findings suggest that the decreasing ratio of postoperative serum AFP is an effective indicator to determine whether or not the lesions were completely extirpated, although a normal value may not always imply the absence of microscopic metastasis of tumor cells. Serial estimation of serum AFP was of value in assessing the presence of recurrences and evaluating the efficacy of chemotherapy. (Author abstract) (12 Refs)

32. ISOLATION OF A URINARY PEPTIDE ASSOCIATED WITH OVARIAN CANCER (MEETING ABSTRACT).

Stenman UH, Huhtala ML, Koistinen R, Seppala M
Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Helsinki, Finland
Oncodev Biol Med; AbstractsBock,1:57 1981

Physicochemical and immunoadsorption techniques were used to prepare an antiserum against a urinary peptide, which occurred in high concentrations in a patient with ovarian cancer. This peptide was isolated by a combination of gel filtration and chromatography on SP-Sephadex and high pressue liquid chromatography on an RP-8 column. The peptide has an apparent mol wt of 7000 and it contains no carbohydrate. Crude preparations of the peptide are microheterogeneous in isoelectric focusing. A radioimmunoassay was developed and the concentration of the peptide in various body fluids determined. In healthy subjects serum contains 30-100 ug/l, urine 30-200 ug/l, urine of newborn infants 100-1500 ug/l, amniotic fluid at 12-18 wk 350-1700 ug/l and at term 50-300 ug/l. In patients with ovarian cancer the concentrations in urine are 300-14000 ug/l and serum levels in the same patients are 50-1500 ug/l. Our results indicate an oncodevelopmental nature of this new peptide. (no Refs)

33. PREGNANCY-ASSOCIATED BETA1-MACROGLOBULIN (BETA1-PAM): A NEW SERUM PROTEIN ASSOCIATED WITH PREGNANCY SERUM-DERIVED IMMUNE COMPLEXES AND OVARIAN CANCER.

Stimson WH, Farquharson DM
Biochemistry Dept., Univ. Strathclyde, 31 Taylor St., Glasgow, G4 0NR, Scotland
J Clin Lab Immunol; 6(2):141-145 1981

A new pregnancy-associated serum protein was found associated with pregnancy serum-derived immune complexes (IC). This protein was partially characterized and shown to be present in the blood of a majority of ovarian cancer patients. IC were obtained from late pregnancy serum and separated into their fractions. An antigen (mol wt range 4-5 x 10(5)) was identified which would consistently recombine with the IgG fraction from dissociated IC. Antisera were raised against the gel chromatographic fraction containing the putative IC component and following exhaustive absorption, were found to be specific for a serum protein with beta1-globulin electrophoretic mobility; this was termed pregnancy-associated beta1-macroglobulin (beta1-PAM). When beta1-PAM levels were estimated in the blood of various groups of subjects, comparatively high concentrations were found in a large proportion of ovarian cancer patients. Late pregnancy sera (40%) were also positive for beta1-PAM, but mostly at levels lower than those found in ovarian cancer, while the serum protein was only detected in 3/186 normal women and 1/62 patients with cervical cancer. Healthy males and subjects with cancer of the breast, colon, and testis were all negative for beta1-PAM. Beta1-PAM preparation obtained from both pregnancy and ovarian cancer sera were found to have the same ammonium sulfate precipitation range and isoelectric point. These data suggested that both beta1-PAM preparations are identical although mol wt values indicate some anomalies. (17 Refs)

34. INTESTINE-ASSOCIATED ANTIGENS IN OVARIAN TUMOURS: AN IMMUNOHISTOLOGICAL STUDY.

de Boer WG, Ma J, Nayman J
Dept. Lab. Medicine, Royal Southern Memorial Hosp., Caulfield South, Victoria 3162, Australia
Pathology; 13(3):547-555 1981

The presence of three intestine-associated antigens, small intestine mucin antig en (SIMA), large intestine mucin antigen (LIMA) and carcinoembryonic antigen (CEA) was studied in the female genital tract and ovarian tumors by immunofluorescence. These antigens could not be detected in normal ovary, benign cysts of ovary, fallopian tube or endometrium, but both LIMA and CEA were present in endocervical glandular tissue. The antigenic cross-reactivity of endocervical and large bowel mucin may indicate a close embryological relationship between these organs during the cloacogenic stage. The three antigens could be demonstrated in mucinous tumors of the ovary but were absent in serous or mesonephroid tumors. In one of the two endometroid tumors CEA was the only detectable antigen. These observations confirm the presence of intestinal type of epithelium in cystic mucinous tumors of the ovary and explain the cross-reactivity of mucin of benign tumors of the ovary and mucin from colonic cancer, normal colonic mucosa and gastric mucosa as reported by earlier workers. In the process of malignant transformation the columnar epithelium of ovarian cystadenoma seems to behave in the same way as superficial gastric and gallbladder epithelium by forming inappropriate intestine-associated mucin substances. Our technique may provide a specific means for studies on the histogenesis of female genital tract tumors, particularly ovarian tumors. It can also be used in differentiating between benign and malignant variants of these tumors. (Author abstract) (15 Refs)

35. STUDIES ON THE DRUG SENSITIVITIES OF HUMAN TUMOUR CELLS OBTAINED DIRECTLY FROM BIOPSY MATERIAL (MEETING ABSTRACT).

Rupniak TH, Marks P, Watkins S, Bourne G, Slevin M, Bancroft-Livingston GH, Simmons CA, Hill BT
Imperial Cancer Research Fund, London, England
Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

We have determined the sensitivities to in vitro drug treatment of tumor cells obtained from the ascitic fluid of patients with ovarian carcinoma. Sensititivity to cis-platinum and adriamycin were assessed using the soft agar clonogenic assay developed by Courtney et al. This procedure gave improved growth of tumor colonies compared to the simpler assay of Salmon et al, and this appeared to be attributable primarily to the use of a low oxygen content gas mixture and a replenishable medium phase. Even so plating efficiencies were often too low and in only 20% of samples provided was there an adequate yield of tumor cells for these tests. The poor clonogenicity of cells from biopsies of a number of solid tumors suggests that this assay has limited applicability for determining specific drug sensitivities of individual patients' tumors. In two patients for whom clinical response could be correlated with in vitro drug sensitivity data, resistance to cis-platinum was observed both in vivo and in vitro, less than 60% cell kill was achieved by a 1 hr exposure to 5 ug/ml cis-platinum - clearly resistant according to the criteria of Salmon et al. These two patients also appeared resistant to adriamycin by the vitro assay (less than 40% cell kill after 1 hr exposure to 1 ug/ml adriamycin - again highly resistant by the criteria of Salmon et al). This is in accordance with clinical experience showing adriamycin to be an ineffective second line drug for ovarian carcinoma. (3 Refs)

36. ADVANCED OVARIAN CARCINOMA: A PROSPECTIVE AND RANDOMIZED CLINICAL TRIAL OF CYCLOPHOSPHAMIDE VERSUS COMBINATION CYTOTOXIC CHEMOTHERAPY (HEXA-CAF).

Carmo-Pereira J, Costa FO, Henriques E, Ricardo JA
Instituto Portugues de Oncologia de Francisco Gentil, 1093 Codex, Lisboa, Portugal
Cancer; 48(9):1947-1957 1981

Fifty-seven evaluable patients with advanced ovarian carcinoma were randomized to receive either a combination of hexamethylmelamine, cyclophosphamide, methotrexate and 5-fluorouracil (Hexa-CAF) or high-dose cyclophosphamide alone given iv intermittently. Objective responses were seen in 62% of patients receiving cyclophosphamide alone, and 36% of patients in the Hexa-CAF regimen, this difference being statistically significant (p less than 0.05). The median duration of objective response (10 mo versus 9 mo) and the median survival (11 mo versus 10 mo) were greater in the cyclophosphamide group, but these differences were not statistically significant. It is concluded that there is no therapeutic advantage for the Hexa-CAF protocol over the alkylating agent used alone. (Author abstract) (27 Refs)

37. CONTINUOUS VS. INTERMITTENT TREATMENT WITH TREOSULFAN IN ADVANCED OVARIAN CANCER (MEETING ABSTRACT).

White WF

St. Luke's Hospital, Guildford, England

Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

Response rates and survival curves are presented for 65 evaluable patients with advanced ovarian cancer (FIGO stages III/IV and abdominal recurrence after surgery), all of whom had visible or measurable disease after laparotomy or biopsy, and who were treated with the cytotoxic agent Treosulfan as the sole chemotherapeutic agent. Two dose regimens were evaluated sequentially. In a continuous regimen, a complete response rate (CR) or 34% and a partial response rate (PR) of 26% was obtained in 35 patients: median survival of those with CR was 19.5 mo, with PR 11 mo, non-reponders 6 mo. In an intermittent regimen, a CR of 47% and a PR of 26% was obtained in 30 patients: median survival of those with CR is greater than 18 mo, with PR 11.5 mo, non-responders 9 mo. In a further group of 16 patients with progressive disease on other chemotherapeutic agents, a response of 38% (CR 19% PR 19%) was obtained: median survival of responders was 15 mo, non-responders 5.5 mo. Dose-limiting toxicity was invariably hematological depression, with moderate falls in Hb and WBC occurring in approx 50% of patients, and thrombocytopenia in 25% of patients. Nausea, vomitting, and hair loss were rarely seen, the commonest side-effect being a generalized pigmentation which occurred in 40% of patients. One patient died from an acute myeloid leukemia 40 mo after commencement of therapy, whilet in complete remission from her ovarian cancer. Treosulfan, administered in an intermittent dosage regimen, appears to have the broadest single-agent activity yet reported in ovarian cancer, and is recommended for further evaluation in other tumors, especially in view of high patient acceptability and minimal side-effects. (no Refs)

38. ADVANCED OVARIAN CARCINOMA: RESPONSE TO ANTIESTROGEN THERAPY.

Myers AM, Moore GE, Major FJ

Div. Hematology, Dept. Medicine, Denver General Hosp., 750 Cherokee St., Denver, CO, 80204

Cancer; 48(11):2368-2370 1981

Three patients with Stage III serous cystadenocarcinoma of the ovary were successfully treated with estrogen antagonist therapy after failure of cytotoxic chemotherapy. All had histologic confirmation of progressive or persistent disease. High titers of estrogen receptor protein (ERP) and progesterone receptor protein (PRP) were detected in one patient prior to tamoxifen therapy. One patient had a complete remission lasting for 18 mo. The other patients had partial responses and were able to return to normal activities. Simultaneous or prior sequential cytotoxic chemotherapy did not negate the effectiveness of the estrogen antagonists. (Author abstract) (6 Refs)

39. PROGESTIN TREATMENT IN ADVANCED EPITHELIAL OVARIAN CANCER (MEETING ABSTRACT).

Mangioni C, La Vecchia C, Franceschi S

1st Obstetrics and Gynecology Clinic, University of Milan, Milan, Italy

Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

From July 1978, 75 patients aged from 28 to 74 yr (median 59) with advanced epithelial ovarian cancer, who had received at least one polychemotherapy regimen, were allocated at random to one of two different medroxyprogesterone acetate (MPA) regimens. Sixty-three patients were evaluable. Thirty-three cases were treated im (500 mg/daily for the first 4 wk; 500 mg twice weekly for the second 4 wk; 500 mg once weekly for the next 4 or more wk). These gave 5/33 (15%) partial responses (PR) (duration 5, 5, 6, 8+ and 6+ mo) and 2/33 stable disease (SD) (duration 3 and 4 mo). The 30 po treated patients (800 mg daily for at least 12 wk) gave no PR, but 2 SD (duration 3 and 3 mo) were obtained. Response was not affec ted by histological grade; endometrioid histotype showed a better responsiveness (2 PR and 2 SD out of 15 patients) but did not reach statistical significance. Overall subjective improvement was noted in 16/63 patients (25%). MPA treatment was well tolerated both by im and po route; only one patient suffered from a gluteal abscess. (no Refs)

TROPHOBLASTIC DISEASE

40. THE VALUE OF RADIOIMMUNODETECTION IN THE MANAGEMENT OF CHORIOCARCINOMA (MEETING ABSTRACT).

Begent RH, Searle F, Stanway G, Jewkes RF, Vernon P, Newlands ES, Bagshawe KD

Departments of Medical Oncology and Nuclear Medicine, Charing Cross Hospital, London, W6 8RF, England

Br J Cancer; 43(5):727 1981

Eighteen patients with human chorionic gonadotropin (hCG) producing tumors (12 gestational choriocarcinoma and 6 malignant teratoma) have been studied by radioimmunodetection (RID), using antibodies directed against hCG. Among 13 patients with positive RID were 3 with drug-resistant choriocarcinoma and opacities in the lung fields on computerized tomography. It was not clear whether these opacities were the site of viable tumor or necrotic tissue. RID was defintely positive at the sites of the opacities in 2 patients and suggestive in the third. Deposits of active tumor were subsequently excised from the relevant area of the lung in these patients, and this appears to have contributed to long-term remission in all 3. By contrast, 3 patients with pulmonary opacities on conventional radiology and negative RID do not appear to have active hCG-producing tumor, as judged by serum hCG measurements and in one case by biopsy. These preliminary results indicate that RID may be of value in management of patients with choriocarcinoma, if it is wished to distinguish between viable and non-viable deposits before surgery. (no Refs)

41. THE ROLE OF VP-16-213 (ETOPOSIDE; NSC-141540) IN MEDIUM RISK GESTATIONAL CHORIOCARCINOMA (MEETING ABSTRACT).

Newlands ES, Bagshawe KD
Charing Cross Hospital, Fulham Palace Road, London W6 8RF, England
Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

Since the introduction of VP 16-213 in patients with drug-resistant gestational choriocarcinoma, we have used this agent as the initial drug in a sub-group of patients. Patients with gestational choriocarcinoma can be ranked accurately on whether the potential for drug resistance is low, medium or high by identifying a number of risk factors. Between 1974 and 1979 we treated 38 patients in the medium risk category. There was only one death from choriocarcinoma but 10 (26%) developed drug resistance and required more intensive chemotherapy and 5 (13%) relapsed off treatment. To 1/2/81 we have treated 32 sequential patients in the medium risk category starting with VP 16-213 100 mg/m2 IV days 1 to 5 and in all these patients there has been a reduction in the Beta Human Chorionic Gonadotrophin (hCG) concentration. Responses have been defined by a fall in the hCG concentration: partial response (PR) is greater than 1 log fall in the hCG concentration and an improvement (IMP) was a greater than 50% fall in the hCG. Using these criteria there have been 11 PR and 13 IMP in these patients. Treatment was continued with hydroxyurea, 6-mercaptopurine, and methotrexate in combination followed by actinomycin-D as a single agent before these patients received VP 16-213 once more. Remissions have been obtained more easily than when patients started on methotrexate as the initial agent, and so far none of the patients achieving complete remission has relapsed off treatment (range 0 to 19 mo). At present this change in treatment appears to combine a reduction in toxicity with greater security of obtaining a complete remission. (2 Refs)

SELECTED PRE-CLINICAL STUDIES

42. PROSTAGLANDIN PRODUCTION BY SQUAMOUS CELL CARCINOMA OF HUMAN UTERINE CERVIX IN VITRO (MEETING ABSTRACT).

Nagasaka T, Winters WD, Soriero OM, Harper MJ
Departments of Obstetrics and Gynecology, University of Texas Health Science Center at San Antonio, San Antonio, TX
International Conference on Prostaglandins and Cancer, August 30-September 2, 1981, Washington, DC. Lombardi Cancer Center 75 pp., 1981.

Production of prostaglandins (PGs) during serial subpassages of 25 newly established squamous cell carcinoma strains of human uterine cervix was measured by radioimmunoassay (RIA). The cells were cultured in 10ml Dulbecco's modified essential medium with 10% fetal bovine serum, 5ug/ml fungizone and 50ug/ml gentamycin added in 75 cm2 plastic flasks. The medium was changed approx every 48 hr and 1 ml aliquots were taken, acidified to pH 4.5 with acetate buffer and extracted with ethyl acetate before RIA. Concentrations of PGE and PGF were significantly lower after the second subpassage than in the initial passage in all cultures tested. However, in all subpassages of the tumor cell strains studied more extensively, there were ten-fold greater amounts of PGE in the culture medium following addition of 10ug/ml of arachidonic acid. PGF levels were unaffected by this amount of arachidonic acid and PGE levels were not increased by amounts of 0.1 or 1.0ug/ml. These results suggest that cells from human squamous cell carcinomas of the uterine cervix possess the synthetic capacity to produce PGs after long-term serial subculture in vitro, but that substrate is depleted. These cell strains may provide a useful model system for future studies on the relationship between PGs and cancer, especially the degree of malignancy and ability to metastasize. (no Refs)

43. MULLERIAN INHIBITING SUBSTANCE INHIBITS GROWTH OF A HUMAN OVARIAN CANCER IN NUDE MICE.

Donahoe PK, Fuller A, Scully RE, Guy SR, Budzik GP
Div. Pediatric Surgery, Massachusetts General Hosp., Boston, MA, 02114
Ann Surg; 194(4):472-480 1981

Mullerian inhibiting substance (MIS) was investigated for its ability to inhibit growth of a human ovarian cancer in nude mice. Biologically active preparations from newborn calf testes, obtained after sequential ion exchange chromatography, delayed or prevented growth of a human ovarian cancer (HOC-21) when 2 x 10(6) cells were preincubated with them prior to sc injection of the tumor cells into Balb/C homozygous nude mice. Preincubation of human colon carcinoma cells (SW-48) with similar preparations of MIS failed to inhibit growth of the tumor cells in nude mice. Human serous carcinomas are thought to arise from the ovarian surface epithelium, a derivative of the coelomic epithelium of the urogenital ridge, which invaginates to form the mullerian duct early in embryonic life. The neoplastic cells of serous tumors simulate morphologically the lining cells of the fallopian tube, which are derivatives of mullerian duct epithelium. this study provides physiologic confirmation of the mullerian nature of this type of tumor and suggests that MIS may ultimately prove to be effective in its therapy. (Author abstract) (37 Refs)

44. EXPERIMENTAL CHEMOTHERAPY WITH HUMAN CHORIOCARCINOMA TRANSPLANTED INTO NUDE MICE AND A CLINICAL STUDY (MEETING ABSTRACT).

Katoh T, Ishige H, Kobayashi O, Takamizawa H, Tokita H, Tanaka N
Department of Obstetrics and Gynecology, Chiba University, Chiba, Japan
Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.

The course of trophoblastic disease except for metastatic choriocarcinoma has improved remarkably. The urgent problem is to obtain an effective chemotherapeutic method for existing drug-resistant patients with metastatic choriocarcinoma. We have been trying to establish new, effective chemotherapy with the experimental model of human choriocarcinoma transplanted into nude mice. Two kinds of human choriocarcinoma, CC-HM-I(HM) and CC-I-JCK(JCK), serially transplanted into nude mice (BALB/c, nu/nu) were treated with methotrexate (MTX), actinomycin D (ACD), cyclophosphamide (CPM), vincristine (VCR), and a bacterial immunopotentiator (OK432) with 1/3 LD50 doses in mice ip once a wk. The effects of the drugs were observed by weekly measurement of tumor size, histological findings, survival rate, and serum human chorionic gonadotropin. All mice with JCK died of tumor around 50 days after transplantation, while the survival rate of mice with JCK treated by ACD+CPM was 100% and the disappearance of tumors was observed. OK432 showed an inhibitory effect on tumor growth. Because of results demonstrated in this study ,

the chemotherapies were administered to two patients. One patient had a remission with negative human chorionic gonadotropin and another patient had 25 per cent regression of pulmonary metastases. (no Refs)

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CERVICAL AND UTERINE TUMORS

1. RADIONUCLIDE LIVER AND BONE SCANNING IN THE EVALUATION OF PATIENTS WITH ENDOMETRIAL CARCINOMA.

Mettler FA, Christie JH, Garcia JF, Baldwin MH, Wicks JD, Bartow SA
Div. Nuclear Medicine, Dept. Radiology, Univ. New Mexico Hosp., Albuquerque, NM, 87131
Radiology; 141(3,part1):777-780 1981

Staging bone scans or skeletal surveys were obtained of 97 patients with endometrial carcinoma. Of the 77 patients with Stage I or II disease, no metastases were identified at staging. Three patients in the entire series demonstrated bony metastases; all of these metastases were detectable by radionuclide bone scan and radiographic bone survey. Eighty-nine patients were examined with radionuclide liver/spleen scanning at the time of staging. Four of the 89 initial scans were interpreted as demonstrating hepatocellular disease, and all four patients had abnormal liver function studies. Only one patient demonstrated a possible hepatic metastasis at initial diagnosis. This patient also had abnormal liver function studies. Based on these results, bone surveys and radionuclide bone scans are not indi-

HE 20.3173/2:

cated as screening procedures in endometrial carcinoma. It is suggested that screening for liver metastases in patients with endometrial carcinoma is not warranted in patients with normal liver function studies. (Author abstract) (15 Refs)

2. THE USE OF COMPUTERIZED TOMOGRAPHY TO OBVIATE CELIOTOMY IN RECURRENT CARCINOMA OF THE CERVIX.

Walton LA, McCartney WH, Vesterinen E
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Gynecol Oncol; 12(2,part1):166-176 1981

CT (computerized tomography) was incorporated into the evaluation of 40 patients with a presumptive diagnosis of recurrent cervical carcinoma. Laparotomy correlation with CT findings was obtained in 15 patients. CT localization of paraaortic or pelvic sidewall disease contraindicated laparotomy for purposes of exenteration in 13 patients. When CT localized recurrent disease to the central pelvis or parametria (12 patients) the need for laparotomy was individualized on the basis of adjunctive studies. (Author abstract) (10 Refs)

3. THE OBSTRUCTED UTERUS.

Scott WW, Rosenshein NB, Siegelman SS, Sanders RC
Dept. Radiology, Johns Hopkins Hosp., 600 Wolfe St., Baltimore, MD, 21205
Radiology; 141(3,part1):767-770 1981

Eleven patients with an obstructed, fluid-filled uterus, due to carcinoma of the uterus or to its treatment by radiation therapy, were examined with computed tomography (CT) and/or ultrasound. It is important to recognize this abnormality to differentiate it from other causes of pelvic mass and to ensure prompt treatment of pyometra, should it develop. Both CT and ultrasound reliably identified this condition and differentiated it from other pelvic masses. (Author abstract) (5 Refs)

4. CERVICOGRAPHY: A NEW APPROACH TO CERVICAL CANCER DETECTION.

Stafl A
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Gynecol Oncol; 12(2,part2):S292-S301 1981

Cervicography (CVG) using a 100-mm macrolens attached to a 35-mm camera body, with a 50-mm extension ring, was used for cervical examination in 728 women. In 28 women, CVG was technically defective. Among the 700 women with satisfactory cervicograms, 296 were referred for colposcopy (CPS) evaluation of abnormal cytologic findings. CVG was negative in 107 patients, unsatisfactory in 47, and suspicious in 142. CPS findings were suspicious in 131 patients and directed biopsies were taken. Histology revealed 5 invasive carcinomas, 2 microinvasive carcinomas, 13 carcinomas in situ, 15 severe dysplasias, 39 moderate dysplasias, and 50 mild dysplasias. In seven cases, histologic findings were negative. The correlation between CVG and biopsy findings in 131 patients with abnormal CPS and CVG findings is presented. Differences in diagnostic accuracy between CPS and CVG were not significant. CVG was within one histologic degree of accuracy in 93.1% of cases and CPS in 92%. In another study of 404 patients who had no previous abnormal cytologic examination, CVG findings were negative in 293 patients, suspicious in 35, and unsatisfactory in 76. Thirty-five patients with suspicious CVG findings were reevaluated by CPS and 26 abnormal lesions were found and a directed biopsy specimen obtained. One case of severe dysplasia, two cases of moderate dysplasia, and six cases of mild dysplasia were detected only by CVG in patients in whom cytologic findings were negative. Advantages of CVG are discussed. (11 Refs)

5. DISCUSSION OF SESSION III: SCREENING OF CERVICAL NEOPLASIA.

Richart RM
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Gynecol Oncol; 12(2,part2):S212-S219 1981

Problem of Papanicolaou smear quality control (QC) was discussed. Issue of QC in cytology is extremely complex and there are no uniformly held criteria for judging a laboratory's quality. Cytological screening for cervical neoplasia should consist of smears taken at 3 yr intervals after two negative smears were obtained 1 yr apart. Prolonged intervals are applicable only to women who had two previous negative examinations. If a prior examination was consistent with dysplasia, the chance of developing invasive cancer in the coming yr is much higher than if the previous examination was entirely negative. Quality of the data available on which to make a judgment regarding the appropriate screening interval was discussed. There is an opinion that prolonged screening intervals could result in increase of the number of women with cervical cancer. (no Refs)

6. APPROPRIATENESS OF CERVICAL CANCER SCREENING.

Eddy DM
Stanford Univ., Stanford, CA, 94305
Gynecol Oncol; 12(2,part2):S168-S187 1981

For the Pap test to be appropriate for the early detection of cervical cancer there should be good evidence that it is effective, its expected benefits should outweigh any risks, and its costs should be reasonable. Although the value of the Pap tests has never been determined in a randomized controlled trial, its effectiveness has been demonstrated indirectly in dozens of clinical and epidemiological studies conducted over the past 3 decades. This paper reviews that evidence. It also examines in detail the effectiveness, costs, and potential risks of delivering the test at various frequencies. Issues discussed include the yield of invasive cancers, the results of large screening programs in which the test was delivered at different frequencies, statistical estimates of the 'cost/effectiveness' of screening at different frequencies, the false-negative rate, laboratory quality control, and the screening of high-risk women. (Author abstract) (77 Refs)

7. PROGNOSTIC VALUE OF CYTOLOGIC EXAMINATION OF PERITONEAL WASHINGS IN PATIENTS WITH ENDOMETRIAL CARCINOMA.

Szpak CA, Creasman WT, Vollmer RT, Johnston WW
(c/o Johnston) Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Acta Cytol (Baltimore); 25(6):640-646 1981

Peritoneal pelvic washings from 54 women with pathologic Stage I endometrial carcinoma were evaluated in a blind retrospective fashion for the concentration of malignant cells present. None of the 42 patients with normal washings developed recurrence after a median disease-free survival of 36 mo. Of the 12 patients with adenocarcinoma in the washings, 4 had high concentrations of malignant cells (greater than 1,000

cells/100 ml sample), and all 4 died as a consequence of carcinoma within 2 yr. The remaining eight patients had lower concentrations of malignant cells in the washings (less than 1,000 cells/100 ml sample), and six of these patients had no evidence of disease after 37 to 64 mo. Cox's nonparametric statistical model showed that increasing concentrations of adenocarcinoma cells in washings significantly shortened the time to recurrence of disease. The abundance of malignant cells has prognostic importance in identifying those patients with pathologic Stage I disease who may require more aggressive therapy. (Author abstract) (32 Refs)

8. PROGNOSTIC FACTORS IN STAGE I CARCINOMA OF THE CERVIX.

Boyce J, Fruchter RG, Nicastri AD, Ambiavagar PC, Reiss MS, Nelson JH
Dept. Obstetrics and Gynecology, Downstate Medical Center, Brooklyn, NY, 11203
Gynecol Oncol; 12(2,part1):154-165 1981

In a series of 177 cases of Stage I epidermoid carcinoma of the cervix, 139 were treated surgically. Increasing depth of invasion of the cervical lesion was associated with greater lateral extension and increasing vascular invasion in the cervix. Increasing depth of invasion in the cervix was significantly associated with (1) increasing incidence of pelvic node metastases, (2) increasing incidence of local extension outside the cervix with negative pelvic nodes, (3) increasing frequency of recurrence, and (4) decreasing 5-yr survival. Patients with extension to the corpus and negative pelvic nodes had poor survival rates. Patients with disease confined to the cervix had poor outcome if the tumor invaded more than 10 mm and was present in vascular spaces. Poor prognostic factors to consider in therapeutic planning are (1) a depth of invasion greater than 10 mm, (2) lateral spread to more than half the cervix, (3) invasion of lymph-vascular spaces in the cervix, (4) spread to the pelvic nodes, and (5) spread to the parametria or corpus uteri. (Author abstract) (16 Refs)

9. CERVICAL CARCINOMA AND EOSINOPHIL. I. EOSINOPHIL CHEMOTACTIC FACTOR DERIVED FROM INVASIVE CERVICAL CARCINOMA WITH EOSINOPHIL INFILTRATION.

Inoue T, Iwasaki K, Chihara T, Torisu M
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Clin Immunol Immunopathol; 21(3):320-331 1981

Surgical specimens from 778 patients with invasive cervical carcinoma were reviewed with respect to eosinophil infiltration. Marked eosinophil infiltration in the tumor was revealed in 78 patients, closely relating to large squamous cell carcinoma, total tumor vol, and preoperative blood eosinophilia. Marked eosinophil infiltrate in regional lymph nodes was found depending upon the degree of eosinophil infiltration in the primary lesion. The tumor extracts from five cases with cervical carcinoma with marked eosinophil infiltration were examined for chemotactic activity. The tumor extracts were highly chemotactic for eosinophils and neutrophils, showing a dose-response fashion in the in vitro and in vivo chemotactic experiments. This eosinophil chemotactic activity was found to be heat-labile and nondialyzable. These findings indicate that this eosinophil chemotactic factor of cervical carcinoma (ECF-CC) may account for the eosinophilic stromal reaction and blood eosinophilia observed in some patients with cancer. (Author abstract) (20 Refs)

10. HERPESVIRUS ANTIGENS AS MARKERS FOR CERVICAL CANCER.

Gupta PK, Aurelian L, Frost JK, Carpenter JM, Klacsmann KT, Rosensbein NB, Tyrer HW
Dept. Pathology, John Hopkins Univ. Sch. Medicine, Baltimore, MD, 21205
Gynecol Oncol; 12(2,part2):S232-S238 1981

A total of 393 patients representing cervical atypias, cancers, and nonneoplastic disease have been studied. Cellular specimens have been stained with antisera raised against total herpes Type 2 virus (HSV-2) and subfractions labeled crude AG-e, pure AG-e, ICP 12, and ICP 14. Reproducibility, statistical significance, false positive and false negative results, specificity, and sensitivity of the various antisera have been investigated. Correlation of immunocytostaining with Papanicolaou staining has been made. Usefulness of these markers in the detection and diagnosis of premalignant and malignant cervical epithelial changes for mass screening has been discussed. Using crude AG-e, pure AG-e, HSV-2, and HSV-1 antisera in a number of blind studies, no significant differences were found in the reproducibility of results. Observations indicated that a minimum of 30 cells must be analyzed to make data amenable to statistical analysis. Exfoliated cells from 62, 75, 77, and 94% of patients respectively diagnosed as mild, moderate, and marked atypia, and cancer were studied with antisera against total HSV-2. Similar results were observed with an tisera against pure AG-e. No patient reacted with anti-AG-e or anti-HSV-1 antiserum in the absence of reactivity to antisera against total HSV-2 antigens. Studies using anti-ICP 12 and -ICP 14 antigens established the wide and specific staining character of anti-HSV-2 antisera. Morphologic preservation of cells by Papanicolaou staining after the FA procedures was considered satisfactory for diagnostic purposes. Our studies indicated the potential usefulness of anti-HSV-2 and anti-AG-e antisera in mass cervical cancer screening programs and cytology automation. (Author abstract) (21 Refs)

11. CARBON DIOXIDE LASER MANAGEMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA.

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Laser Res. Foundation, 3439 Kabel Dr., New Orleans, LA, 70114
Am J Obstet Gynecol; 141(7):828-832 1981

In this report we describe the use of the carbon dioxide laser for the outpatient management of cervical intraepithelial neoplasia (CIN). A comparison of treatment effectiveness for different grades of CIN is also included. Two hundred fifty-six cases were evaluated by colposcopy, cytology, and histopathology, treated by at least 5 to 6 mm of laser vaporization, and followed up for an av of 10.7 mo. Follow-up examinations included cytology, colposcopy, and directed biopsy if a suspicious lesion was discovered. During the follow-up, 18 cases of persistent CIN were identified (7.0%). Most of these were successfully managed with repeat laser treatment. Overall success of laser surgery for CIN, one or two applications, was 97.6%. Few complications were encountered. Laser surgery appears to offer acceptable treatment effectiveness, early identification of persistent disease, and easy retreatment when required. (Author abstract) (7 Refs)

12. ONGOING CLINICAL TRIALS IN CERVICAL INTRAEPITHELIAL NEOPLASIA BY THE GYNECOLOGIC ONCOLOGY GROUP.

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Gynecol Oncol; 12(2,part2):S302-S305 1981

Two protocols of the Gynecologic Oncology Group (GOG) dealing with Phase III trials in patients with cervical intraepithelial neoplasia (CIN) are described. Protocol 31-GOG is a randomized comparison of the immediate and long-term effectiveness of outpatient cryosurgery and outpatient local excision in treatment of limited CIN, Grades I, II, or III, administered within 12 wk of diagnosis. Observations and tests during follow-up will include cervical cytology 4 and 8 mo after treatment, and every 6 mo in the absence of CIN for 2 yr post-treatment, and annually for the following 3 yr. Recurrence is defined as two consecutive abnormal PAP smears. Protocol 32-GOG is a randomized comparison of the immediate and long-term effectiveness of outpatient cryosurgery compared to in-hospital standard cold-knife conization in the treatm ent of extensive, Grade III, CIN. Patients must be randomized within 12 wk of diagnosis. All patients must have lesions that can be delineated through the colposcope; lesion or lesions must involve at least two quadrants of the portio with at least one quadrant diagnosed as CIN-III. At least three directed biopsies must be taken and the endocervical curettage must be negative for CIN. Observations, tests, and criteria for defining recurrence or persistence will be the same as in protocol 31. (no Refs)

13. RESULTS OF OUTPATIENT THERAPY OF CERVICAL INTRAEPITHELIAL NEOPLASIA.

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Gynecol Oncol; 12(2,part2):S306-S316 1981

Failures of the outpatient therapy of cervical intraepithelial neoplasia (CIN) and results of different treatment modalities are reviewed. Failures are considered in relation to histology, size and location of lesion, and depth of destruction. These four areas of concern must be addressed when outpatient therapy is contemplated. In an early series, 89% of 182 women with dysplasia were cured by one application of electrocautery. In another study of electrocautery, failure rate was 13.6% in 88 patients with CIN-III. Success rate in a group of studies on cryosurgery published in 1980 ran from 27 to 96%. Variations in results were attributed to many factors, including the experience of the operator, numbers treated, criteria employed, as well as freezing techniques, equipment and refrigerant. A continuing concern with this technique remains the variability of the freeze, particularly as it relates to destruction of disease in endocervical crypts. Five studies with laser therapy show a failure rate that is higher than with cryosurgery or electrocautery. While it was thought that laser therapy limited to the exact lesion, as delineated colposcopically, would spare the rest of the cervix, the failure rate has been high. As the depth of destruction with laser therapy has increased, failure rate has decreased. A continuous beam has given better results than an intermittent beam. A new modality, the 'cold' coagulator, which uses a lower temperature than electrocautery but is still capable of tissue destruction, has been introduced for outpatient treatment of CIN. (30 Refs)

14. A MODIFIED DOSE MONITORING SYSTEM IN REMOTE AFTERLOADING THERAPY OF CARCINOMA OF THE UTERINE CERVIX USING SEMI-CONDUCTOR DOSIMETER.

Inoue T, Inoue T, Harada K, Hata K, Ozawa R, Kawanabe K
Dept. Radiation Therapy, Center for Adult Diseases Osaka, Nakamichi, Higasinari-ku, Osaka 537, Japan
Strahlentherapie; 157(6):400-404 1981

A dose monitoring system in high dose rate intracavitary remote afterloading therapy of carcinoma of the uterine cervix using semiconductor dosimeter was developed in July 1979 at our d epartment. During early experience with the above system, extremely high values of mgh as well as high doses to rectum and bladder were encountered in the cases with poor local anatomy or unsuitable application. Solving this problem, some limitations as to the mgh as well as point-A dose were added to the computerized rapid processing system for the pre-treatment dose calculation and correction of the treatment parameters to adjust the point-A dose to within +-5% of the planned dose. In the majority of the cases treated with Ralstron, this modified dose monitoring system brought considerable success in the optimization of point-A dose, mgh, rectal and bladder doses, in a simple manner. (Author abstract) (15 Refs)

15. LATE SILENT COMPLICATIONS AFTER TREATMENT OF UTERINE CANCER.

Suramo I, Kauppila A, Lanning P
Dept. Radiology, Univ. Central Hosp., Oulu, Finland
Int Surg; 66(3):251-253 1981

Forty-one symptom-free women treated by operative and irradiation therapy for gynecological cancer 24-108 mo previously were examined by small bowel barium meal, large bowel barium enema, iv urography and renography in order to determine whether there were any silent complications present after the therapy. It was possible to demonstrate intestinal or urological damage by roentgenological examinations in 12 patients. Small bowel changes were found in 5 and large bowel changes in 6 patients, while 8 had changes in urography and 18 in renography. Two intestinal and four urological changes were moderate or severe. These findings indicate that a careful follow-up program regarding complications and recurrences is necessary. (Author abstract) (8 Refs)

16. MEDROXYPROGESTERONE ACETATE (MPA) PLASMA LEVELS AFTER ORAL AND INTRAMUSCULAR ADMINISTRATION IN A LONG-TERM STUDY.

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Dept. Gynecological Oncology, Univ. Hosp., S - 750 14 Uppsala 14, Sweden
Acta Obstet Gynecol Scand [Suppl]; (101):65-70 1981

In a long-term study (1 yr) the plasma concentration of medroxyprogesterone acetate (MPA, Depo-Provera, Provera, Upjohn) was measured in 30 patients with endometrial carcinoma treated with MPA in the following dosages: (1) MPA 1,000 mg im weekly, (2) MPA 1,000 mg im once every second wk, and (3) MPA 100 mg po bid. In the orally treated group the blood samples were taken just before the next tablet. The plasma concentration in the orally treated group rapidly reached steady state, while the im treated group showed gradually increasing levels that had a tendency to level off after 6 mo. The mean concentration at the end of the yr was about 3x higher for MPA 1,000 mg im weekly than for MPA

100 mg po bid. This does not take into consideration the peak MPA level that occurs 2-4 hr after each tablet. MPA im has a very good depot effect, with release of MPA from the injection site for up to 9 mo. The steady initial i ncrease in MPA plasma concentration seen in the im treated groups is probably due to the additions of new depots rather than accumulation in the body generally. (Autbor abstract) (13 Refs)

17. ACTION OF MPA IN ENDOMETRIAL ADENOCARCINOMA. CLINICAL RESULTS AND ULTRASTRUCTURAL AND HISTOCHEMICAL STUDY.

Pulle C, Rigano A
Istituto di Clinica Ostetrica e Ginecologica, Universita degli Studi di Messina, Messina, Italy
Minerva Ginecol; 33(10):937-954 1981

Of 113 endometrial adenocarcinoma patients, 36 (Group A) who were in Stage I and who had not received previous hormonal treatment were administered medroxyprogesterone acetate (MPA: 1 g/day, im) for 3 wk before surgery, 54 (Group B) who were in Stage I received the MPA (1 g/wk) immediately after surgery, and 23 (Group C) who were in advanced stages, and who could not have surgery received the MPA (1 g/dose) on alternate days up to 10 g, then 1 g/wk indefinitely. One-, 3-, and 5-yr survival rates were 36/36, 33/36, and 31/36, respectively, for Group A; 54/54, 46/54, and 41/54 for Group B; and 19/23, 15/23, and 4/23 for Group C. Relapse rates after 1, 3, and 5 yr were 0/36, 2/36, and 4/36 for Group A; 4/54, 7/54, and 5/54 for Group B; and 4/23, 9/23, and 9/23 for Group C. Enzymatic and ultrastructural changes (cell apex, microvilli, ciliary apparatus, plasma membrane, cellular membrane, mitochondria, ribosomes, chromatin, desmosomal apparatus, cytoplasmic organelles, and nucleus) were observed in tumor cells of the patients who had been treated with MPA, indicating secretory activity in almost all of the cells; this activity was nearly absent in tumor cells of the untreated patients. The changes appeared to reveal an attempt of the neoplastic cell to return to normal cellular form and function. (58 Refs) (In ITA)

18. HORMONAL AND CYTOTOXIC CHEMOTHERAPY FOR ENDOMETRIAL CARCINOMA. STEROID RECEPTORS IN THE SELECTION OF APPROPRIATE THERAPY.

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Acta Obstet Gynecol Scand [Suppl]; (101):59-64 1981

Progestin therapy yields an objective remission in about one-third of patients with advanced endometrial carcinoma. Cytotoxic chemotherapy has also clearly proved effective in recent yr, and anti-estrogen therapy to an indicative degree. It is remarkable that both these therapies appear to exert their antineoplastic effect even in patients unresponsive to progestin. A survey of current knowledge on estrogen (ER) and progestin receptors (PR) demonstrates that they are present simultaneously in 41-80% of samples of endometrial carcinoma tissue. The concentration of cytosol ER and PR tends to decrease from well differentiated towards anaplastic carcinomas. This indirect evidence, together with some preliminary clinical observations, suggests that an absence or low concentration of ER and/or PR is s uggestive of a poor prognosis. It is thought that an assay of ER and PR might be of value in predicting the response to chemotherapy in endometrial carcinoma, such as in breast carcinoma. This does indeed seem to be the case, as at least four independent clinical studies have to date confirmed that significant amounts of cytosol ER alone, and especially cytosol PR alone, or both together, in the tumor tissue can predict with reasonable accuracy a good sensitivity to progestin. In like manner, a low cytosol concentration of these steroid receptors appears to predict a good response to cytotoxic chemotherapy, as demonstrated in one study. Progestin and anti-estrogen exert their anti-neoplastic effect via an operative receptor mechanism in different ways, whereas cytotoxic chemotherapy acts by means not involving steroid receptors. It is therefore likely that a detailed characterization of the endocrine relations of the tumor by precise assay of ER and PR from the cytosol and nuclear fractions, together with determination of the end-product of progestin action, 17beta-hydroxysteroid dehydrogenase, will further enhance the accuracy of individual a priori selection of the most efficacious chemotherapy available. (Author abstract) (55 Refs)

19. INFLUENCE OF HUMAN LEUKOCYTE INTERFERON ON SQUAMOUS CELL CARCINOMA OF UTERINE CERVIX: CLINICAL, HISTOLOGICAL, AND HISTOCHEMICAL OBSERVATIONS. III. COMMUNICATION.

Krusic J, Kirhmajer V, Knezevic M, Ikic D, Maricic Z, Rode B, Jusic D, Soos E
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J Cancer Res Clin Oncol; 101(3):309-315 1981

Fifteen patients (23-55 yr old) with squamous cell carcinoma of the cervix (2 Grade I A, 10 Grade I B, and 3 Grade II B) were treated with human leukocyte interferon (HLI) topically (6 patients: 2 x 10(6) daily units with the contraceptive pessary) alone or with im HLI injections (9 patients: 1 x 10(6) units). HLI was administered for 21 days in 14/15 patients and for 40 days in 1/15. Upons completion of HLI treatment, the patients underwent surgery and/or radiation. After HLI therapy, the tumor regressed 1/3 in size; papillary structures also disappeared from the tumor surface and it was eventually covered by smooth fibrous membrane. At surgery, the peritoneal blood vessels and regional lymph nodes were found to be enlarged. Metastases were observed in only one patient. Would-healing and postoperative course were normal in all 15 patients. No significant difference in response to therapy was noted in patients treated topically and those treated topically and im. Based on stromal response, relationship between tumor cell and macrophage activity, and degree of regional lymph node reactivity, the overall response induced by HLI therapy was considered excellent in 6/15 patients, very good in 5/15, moderate in 1/15, poor in 2/15, a nd no response in 1/15. Tests made for bacterial antigens showed that the anamnestic immunologic response did not change essentially under the influence of HLI. At 11-34 mo follow-up, no local recurrence or distant metastases were detectcd in 14/15 patients. (6 Refs)

20. INTERFERON TREATMENT OF UTERINE CERVICAL PRECANCEROSIS.

Ikic D, Singer Z, Beck M, Soos E, Sips D, Jusic D
Inst. Immunology, Rockefellerova 2, YU-41000 Zagreb, Yugoslavia
J Cancer Res Clin Oncol; 101(3):303-308 1981

Groups of patients with cervical intraepithelial neoplasia (CIN) were randomly selected for treatment with human leukocyte interferon (13 patients with CIN, Grade I and II) or placebo (18 patients with CIN, Grade I-III). Follow-up studies at 2 yr showed significant differences between the treated and placebo groups with regard to cytologic findings and pathohistological diagnoses. In the controls, the pathologically changed

epithelium was persistent in 7/18 cases and there were 7/18 progressions. Among the controls, no regressions were observed. In the patients treated with human leukocyte interferon (HLI), abnormal epithelium persisted in 4/13 cases, progressed in 1/13, and regressed in 8/13. In the control and HLI-treated groups, significant progressions and regressions, respectively were observed in relation to morphogenesis of cervical carcinoma. The differences were greater when the groups were compared. The results indicated that HLI has an impact on the regression of cervical intraepithelial neoplasia. Therapy with HLI is particularly indicated in women in the reproductive age in whom fertility is to be preserved since it may obviate the need for surgery. (10 Refs)

21. DIETARY VITAMIN C AND UTERINE CERVICAL DYSPLASIA.

Wassertheil-Smoller S, Romney SL, Wylie-Rosett J, Slagle S, Miller G, Lucido D, Duttagupta C, Palan PR
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Am J Epidemiol; 114(5):714-724 1981

A case-control study of women with cervical abnormalities identified through Pap smears, was conducted in the Bronx, New York, to explore the relationship between nutritional intake and cervical dysplasia. Nutrient intake was estimated from computer analysis of 3-day food records and 24-hr recall for 169 study participants (87 cases, 82 controls), including a subset of 49 pairs matched for age, race and parity. Mean vitamin C intake per day from 3-day food record for controls was 107 mg, compared to 80 mg for cases (p less than 0.01). Analysis of matched pairs showed similar results; 29% of cases compared to 3% of controls in matched subset had vitamin C intake less than 50% of the recommended daily allowance, yielding a 10-fold increase in risk of cervical dysplasia as estimated by odds ratio (p less than 0.05). Younger age, greater frequency of sexual intercourse and younger age at first intercourse were associated with higher risk of cervical dysplasia. Multiple logistic analyses indicated that low vitamin C intake is an independent contributor to risk of severe cervical dysplasia when age and sexual activity variables are controlled. Approx 35% of US women in their reproductive yr have daily vitamin C intake below 30 mg, and 68% have vitamin C intake below 88 mg. If other studies confirm these findings, it may be important to explore a possible protective role of supplementary vitamin C for women at high risk of cervical cancer. (Author abstract) (31 Refs)

22. ETIOLOGICAL CONCEPTS IN CERVICAL CARCINOGENESIS.

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Gynecol Oncol; 12(2,part2):S7-S24 1981

Current evidence on etiology of human cervical neoplasia (CN) was reviewed. Epidemiological factors of possible etiological significance are coitus, marriage, pregnancy, penile factors, syphilis, trichomoniasis, and herpesvirus genitalis (HVG). Seroepidemiologic studies of herpesvirus type 2 (HSV-2) gave indirect evidence of its etiologic role in human CN. Squamous carcinoma of the cervix behaves as a venereal disease. Findings suggest that certain males having venereal diseases may transmit a risk factor for CN by coital contacts. A necessary condition is that certain females are receptive hosts for the putative venereal carcinogen. Risk factor in females is associated with steroid hormone balance (estrogenic hormones). A virion polypeptide AG-4 associated with the active growth phases of CN and a structural component of the HVG, AG-e was identified and isolated. (81 Refs)

23. HUMAN PAPILLOMAVIRUS AND CANCER OF THE UTERINE CERVIX.

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Gynecol Oncol; 12(2,part2):S111-S123 1981

Human papillomavirus infection of the cervix was found in 1.69% of 234,715 women during a mass screening program during the years 1975 to 1979 inclusive. Condylomata of the cervix represent the most prevalent squamous lesion diagnosed during this 5-yr period. Most of condylomata (71.16%) were found in women under 30 yr of age with a mean of 27.47 yr and a peak incidence of 2.5% in the 20-25 yr-age group. Condylomata precede invasive carcinoma by 27.45 yr. The coexistence of condylomata was observed in 25.6% of dysplastic and neoplastic lesions. This association seems to shorten the mean time for malignant transformation. The epidemiologic behavior of condylomata appears similar to dysplasia which is considered a precursor of neoplasia. However, the high regression rate of condylomata (68.39%) implies that lowered immunity and other promoting or synergistic factors are necessary for malignant conversion. (Author abstract) (123 Refs)

24. GENITAL CANCER AND VIRUSES.

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Gynecol Oncol; 12(2,part2):S25-S41 1981

Current data suggesting an association between viruses and genital cancer are reviewed. The main emphasis is on the relationship between herpes simples virus Type 2 (HSV-2) and cervical cancer. Seroepidemiological studies are presented along with emphasis on HSV-transforming and oncogenic potential. Although the evidence is indirect, it is highly suggestive. HSV-2 has the oncogenic potential to produce neoplastic disease in animals. The ability of HSV-2 to transform cells in vitro and for transformed cells to produce tumors in vivo is presently the most direct evidence for oncogenic potential. In vivo experiments, more closely linking HSV-2 and cervical cancer are hampered by the severe cytopathic effect of HSV-2. Evidence associating two other viruses, human cytomegalovirus (CMV) and human papilloma virus (PV), with cervical and prostatic cancer are also discussed. Factors associating CMV with genital cancer include the establishment of persistent infections of the genitourinary tract, transmission by sexual contact, seroepidemiological studies with antibodies and genital cancer, detection of virus particles or virus-specific antigens in genital cancer biopsies, and in vitro transformation studies. Factors associating PV with genital cancer include association with venereal disease, conversion of condylomata acuminata to malignant state, and detection of genital carcinoma within condylomata. (97 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

25. STUDY OF THE METASTATIC SPREAD VIA THE RETROPERITONEAL ROUTE BY MEANS OF LYMPHOGRAPHY.

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Instituto Nazionale Per Lo Studio E La Cura Dei Tumori, Via Venezian 1, 20133 Milano, Italy
Radiol Diagn (Berl); 22(4):521-524 1981

The results of lymphographic (LG) study of 365 cases of ovarian carcinoma (OC) and 48 cases of dysgerminoma are reported. OC spread by three routes: (1) direct invasion of contiguous tissue, (2) diaphragmatic lymphatic spread to retrosternal and mediastinal nodes, and (3) lymphatic spread to retroperitoneal nodes. Metastases were found by LG in 30.7% of carcinoma patients, including 26.4% of new cases and 37.2% of restaged cases. Lymph node involvement (LNI) was found in 53.1% of undifferentiated, 35.1% of serous, 28.4 % of endometrioid OC, 21% of unclassifiable, 10.9% of mucinous, and 9.1% of clear-cell OC. LNI was found in 35.4% of new and restaged dysgerminoma, reflecting the greater tendency of this disease to lymphatic metastasis. Contrary to anatomic studies, results of LG indicate that lymphatic spread of ovarian tumors occurs equally by all lymphatic trunks, rather than predominantly by the gonadal pathway. LG showed a 93.2% correlation with histologic diagnosis, a sensitivity of 100%, and a specificity of 84%. Site of metastasis could not be predicted even in early stages of disease. (2 Refs)

26. LYMPHATIC METASTASIS IN APPARENTLY EARLY CARCINOMA OF THE OVARY.

Metz SA, Sevin BU, Averette HE, Karnei RF, Hoskins WJ
Dept. Obstetrics, Gynecology, Natl. Naval Medical Center, Bethesda, MD, 20014
Gynecol Oncol; 12(2,part1):261-267 1981

Direct extension of ovarian carcinoma to contiguous structures and intraabdominal involvement via dissemination of exfoliated tumor cells is well recognized. The importance of metastatic spread via abdominal and pelvic lymphatics, especially in the absence of other forms of spread, is less well described. In this report we present two patients with ovarian carcinoma in whom widespread lymphatic metastasis was found to have occurred early in the course of the disease process. Neither of these patients exhibited obvious ip spread of their disease at time of initial surgery. Each was, in fact, considered by her referring physician to have Stage I disease. Recent literature pertinent to early retroperitoneal spread of ovarian malignancy is discussed, and the importance of thorough systematic evaluation of potential sites of metastasis during surgical staging is stressed. (Author abstract) (16 Refs)

27. TREATMENT OF CHEMOTHERAPY-RESISTANT ADVANCED OVARIAN CANCER WITH A COMBINATION OF CYCLOPHOSPHAMIDE, HEXAMETHYLMELAMINE, ADRIAMYCIN, AND CIS-DIAMMINEDICHLOROPLATINUM (CHAP).

Bruckner HW, Cohen CJ, Deppe G, Kabakow B, Wallach R, Ratner L, Holland JF
Dept. Neoplastic Diseases, Mount Sinai Hosp., Mount Sinai Sch. Medicine, New York, NY, 10029
Gynecol Oncol; 12(2,part1):150-153 1981

A four-drug regimen consisting of cyclophosphamide, hexamethylmelamine, adriamycin, and cis-diamminedichloroplatinum (II) (CHAP) produced three complete clinical and seven partial responses for 21 patients with adenocarcinoma of the ovary after objective progression of disease during treatment with standard chemotherapy. Median survival was 15 mo for responders and 7 mo for all patients. (Author abstract) (10 Refs)

28. THE ROLE OF HEXAMETHYLMELAMINE IN ADVANCED OVARIAN CARCINOMA TREATMENT.

Weiss RB
Cancer Therapy Evaluation Program, Div. Cancer Treatment, NCI, Bethesda, MD, 20205
Gynecol Oncol; 12(2,part1):141-149 1981

Hexamethylmelamine has been in clinical trial for about 17 yr. A New Drug Application for marketing of this drug has recently been submitted to the US Food and Drug Administration. This paper reviews the efficacy of hexamethylmelamine as a single drug and in combination with other drugs in the treatment of advanced ovarian carcinoma. It appears to be a useful part of several highly effective combination drug regimens in current use. The drug's side effects and dose schedules are also reviewed in detail. (Author abstract) (27 Refs)

29. CHEMOTHERAPY OF MALIGNANT OVARIAN TUMOR; RESULTS OF THERAPY WITH IFOSFAMIDE.

Yakushiji M, Tsunawaki A, Nishida T, Nishimura H, Natsuaki Y, Inoue T, Kato T
Dept. Obstetrics and Gynecology, Kurume Univ., Sch. Medicine, Kurume-shi, Fukuoka Pref. 830, Japan
Nippon Sanka Fujinka Gakkai Zasshi; 33(7):1071-1076 1981

The effect of ifosfamide on primary ovarian malignancies in 30 patients who were treated at Kurume University Hospital from September 1978 to December 1980 are reported. These cancers were advanced or recurrent, and histologically they consisted of serous cystadenocarcinoma in 22 cases, mucinous cystadenocarcinoma in 2, unclassified adenocarcinoma in 1, and malignant teratoma in 5. In the ifosfamide therapy, 2 g or 40 mg/kg per day were given iv for 5 consecutive days, and while the blood state and the general condition were observed, it was repeated every 3 wk. The drug was given in from one to seven courses (av 3.3 courses). The effect was evaluated by Koyama-Saito's criteria and Karnofsky's criteria; the response rate was 48% in the adenocarcinoma group and 20% in the malignant teratoma group according to the former criteria, while it was 64% and 20%, respectively, according to the latter criteria. Hemorrhagic cystitis, nausea and vomiting were the main side effects, and myelotoxicity was low. (16 Refs)

30. IMPACT OF CISPLATIN MULTIAGENT CHEMOTHERAPY AND TOTAL PARENTERAL HYPERALIMENTATION ON BOWEL OBSTRUCTION CAUSED BY OVARIAN CANCER.

Tunca JC
Dept. Obstetrics and Gynecology, Univ. Wisconsin Center Health Sciences, 600 Highland Ave., Madison, WI, 53792
Gynecol Oncol; 12(2,part1):219-221 1981

Seven ovarian cancer patients with complete bowel obstruction were treated with cisplatin combination chemotherapy and total parenteral hyperalimentation. The av time for hyperalimentation was 44.5 days. Six of the seven patients responded to therapy and were discharged from the hospital. This kind of therapeutic modality has value especially for single-agent chemotherapy failure in ovarian cancer with intestinal obstruction. (Author abstract) (3 Refs)

31. A STUDY OF ESTROGEN AND PROGESTERONE CYTOSOL RECEPTOR CONCENTRATION IN BENIGN AND MALIGNANT OVARIAN TUMORS AND A REVIEW OF MALIGNANT OVARIAN TUMORS TREATED WITH MEDROXYPROGESTERONE ACETATE.

Bergqvist A, Kullander S, Thorell J
Dept. Obstetrics and Gynecology, Malmo Allmanna Sjukhus, S - 214 01 Malmo, Sweden
Acta Obstet Gynecol Scand [Suppl]; (101):75-81 1981

ER and PR were assayed in 13 malignant and 20 benign ovarian tumors of different histologic types. ER was detectable in 67% and PR in 40% of the malignant tumors, compared with 35 and 45% in the benign tumors, respectively. The ER concentration was somewhat higher in the malignant lesions but there was no difference in the PR level. A retrospective review of 39 primary ovarian tumors of different pathologic stages and classes, treated postoperatively with medroxyprogesterone acetate (MPA, Depo-Provera, Upjohn) and in most cases Melphalan, showed a high Karnofsky performance index and good complete and partial response rates. The need for a prospective, controlled study of the role of MPA treatment of malignant ovarian tumors is evident. (Author abstract) (33 Refs)

32. OVARIAN TUMORS IN CHILDREN AND ADOLESCENTS.

Yakushiji M, Matsukuma T, Abe M, Nishida T, Nishimura H, Tsunawaki A, Kato T
Dept. Obstetrics and Gynecology, Kurume Univ., Sch. Medicine, Kurume-shi, Fukuoka Pref. 830, Japan
Nippon Sanka Fujinka Gakkai Zasshi; 33(6):833-838 1981

Seventy-six cases of ovarian neoplasms in persons under 20 yr old who had been treated at the Kurume University Hospital from January 1952 through December 1980 are presented. The incidence of ovarian tumors was 5.5% in all age groups; the youngest patient was 5 yr old and the mean age was 15. Histologically 48 (63%) of these tumors were of germ cell origin, a characteristic property of ovarian tumors occurring in childhood and adolescence. The 76 cases included 40 of malignant tumors, which were subdivided into 13 of embryonal carcinoma, 12 of solid teratoma, 9 of dysgerminoma, 5 of simple carcinoma, and 1 case of granulosa cell tumor. In all the cases the clinical stage was an important factor for prognosis, and the prognosis for embryonal carcinoma was poorest, with only 4 of 13 patients surviving. However the prognosis for dysgerminoma was comparatively good, with eight of nine patients surviving. It is worthy of note that this tumor was highly radiosensitive, since three of four patients at Stage III or IV survived for over 5 yr. (Author abstract) (32 Refs)

33. OVARIAN CARCINOMA COMPLICATED BY GASTRIC OUTLET OBSTRUCTION.

Katz LB, Frankel A, Cohen C, Slater G
(c/o Slater), Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY, 10029
J Surg Oncol; 18(3):261-264 1981

Two patients with gastric outlet obstruction secondary to ovarian carcinoma are presented. The importance of considering this complication in an obstructed patient with known ovarian carcinoma is emphasized. Treatment of this condition by gastroenterostomy can lead to significant palliation, as well as allow further treatment of the primary disease by other modalities such as chemotherapy. (Author abstract) (9 Refs)

34. INCIDENCE OF OVARIAN CANCER IN RELATION TO THE USE OF ORAL CONTRACEPTIVES.

Weiss NS, Lyon JL, Liff JM, Vollmer WM, Daling JR
Dept. Epidemiology and Biostatistics, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Int J Cancer; 28(6):669-671 1981

Female residents of six counties in Washington and Utah in whom a diagnosis of ovarian cancer was made during 1975-79 were interviewed concerning prior use of oral contraceptives. Interviews with a random sample of women drawn from these same counties were obtained for comparison. A smaller proportion of women with epithelial ovarian tumors had taken oral contraceptives than had controls: the estimated risk of ovarian cancer in users relative to that in non-users was 0.57 ($p = 0.04$). The magnitude of the decreased risk depended on the duration over which oral contraceptives had been taken, as the negative association was present only after 4 or more yr of use. In many ways, the use of oral contraceptives mimics the physiologic effects of pregnancy. The results of the present investigation, when interpreted together with those from other epidemiologic studies and from experiments in animals, suggest that, like pregnancy, the use of oral contraceptives has a protective effect against the development of ovarian cancer. (Author abstract) (14 Refs)

TROPHOBLASTIC DISEASE

35. CEREBROSPINAL FLUID HUMAN CHORIONIC GONADOTROPIN LEVELS IN NORMAL PREGNANCY AND CHORIOCARCINOMA.

Berkowitz RS, Osathanondh R, Goldstein DP, Martin PM, Mallampati SR, Datta S
New England Trophoblastic Disease Center, Div. Gynecologic Oncology, Brigham and Women's Hosp., Boston, MA
Surg Gynecol Obstet; 153(5):687-689 1981

We measured human chorionic gonadotropin levels simultaneously in the serum and cerebrospinal fluid of 36 normal pregnant women and of 6 patients with choriocarcinoma. During normal pregnancy, human chorionic gonadotropin levels in the cerebral spinal fluid correlated well with those in the serum in both the first and third trimesters. A serum-cerebral spinal fluid human chorionic gonadotropin ratio of less than 60 has previously been reported as a sensitive diagnostic test for trophoblastic CNS involvement. However, we found this ratio to be less than 60 in one patient undergoing first trimester abortion and in one patient with nonmetastatic choriocarcinoma. Furthermore, two patients with documented trophoblastic cerebral metastases had serum-cerebral spinal fluid human chorionic gonadotropin ratios in excess of 60. Results of our study, thus, indicate that determination of a single serum-cerebral spinal fluid human chorionic gonadotropin ratio may not conclusively prove or exclude trophoblastic CNS metastases. Unless it is corroborated by other diagnostic means, a single decreased serum-cerebral spinal fluid human chorionic gonadotropin ratio is insufficient evidence to initiate multimodality treatment for presumptive CNS involvement. (Author abstract) (3 Refs)

36. RECURRENT GESTATIONAL TROPHOBLASTIC DISEASE.

Surwit EA, Hammond CB
Univ. Arizona Health Sciences Center, Tucson, AZ, 85724
Gynecol Oncol; 12(2,part1):177-185 1981

A retrospective analysis of all patients treated at Duke University Medical Center for recurrent malignant gestational trophoblastic disease is presented. Four patients (3%) with nonmetastatic disease developed recurrent tumor in the uterus from 1 mo to 3 yr after achieving primary remission. Eleven patients (26%) in the poor prognostic category developed recurrences from 1 to 12 mo after achieving primary remission. Liver metastases, previous chemotherapy, and a significant delay from the antecedent gestational event were identified as risk factors for the development of recurrent disease in this high-risk group. Aggressive initial chemotherapy and continued treatment after a negative titer is achieved are advocated to reduce the likelihood of recurrent disease in these patients. (Author abstract) (15 Refs)

37. CASE REPORT: TROPHOBLASTIC PSEUDOTUMOR - EVIDENCE OF MALIGNANT DISEASE POTENTIAL.

Twiggs LB, Okagaki T, Phillips GL, Stroemer JR, Adcock LL
Dept. Obstetrics and Gynecology, Univ. Minnesota Medical Sch., Minneapolis, MN, 55455
Gynecol Oncol; 12(2,part1):238-248 1981

Trophoblastic pseudotumor, the histopathologic entity described by Kurman and associates has been considered in the scheme of gestational trophoblastic neoplasia as an exaggerated form of syncytial endometritis and, therefore, associated with a benign outcome. The manifestation of malignant sequalae and ultimate demise of a patient in a recognized case of trophoblastic pseudotumor is presented. Light and electron microscopic studies and autopsy findings are discussed. Therapies, both surgical and chemotherapeutic, and serum assay of the beta subunit of human chorionic gonadotropin are correlated to the clinical course. (Author abstract) (10 Refs)

MULTI-SITE STUDIES AND REVIEWS

38. INTERSTITIAL IRRADIATION IN RECURRENT GYNECOLOGICAL CANCER.

Nori D, Hilaris BS, KimHS, Clark DG, Kim WS, Jones WB, Lewis JL
Brachytherapy Service, Dept Radiation Therapy, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Int J Radiat Oncol Biol Phys; 7(11):1513-1517 1981

From 1957 to 1976, 96 patients with recurrent gynecological cancers documented by biopsy underwent interstitial implantation. Group I (75 patients) had recurrent cervical cancer and Group II had various other recurrent gynecological cancers (7 endometrial, 6 ovarian, 3 vulvar, 5 others). Of the patients in Group I, 74 had epidermoid carcinoma, and one had an adenocarcinoma. Permanent interstitial implants included Ir-192 in 39 patients, Rn-222 in 12, Au-198 in 1, and I-125 in 23. Various surgical procedures were also performed and patients received post-operative external pelvic radiation. Ten patients experienced transient early complications, and five had late complications requiring surgical intervention. One yr after implantation, 34/75 (45%) were alive and disease-free after implantation and 7 patients were alive and disease-free at 5 yr after treatment. Median survival was 11 mo. Patients with disease limited to the vagina, cervix, or periurethral region had better median survival (18 mo) and 5 yr survival (31%). The 5-yr survival of patients with positive nodes was 3% and 7% for those with negative nodes. Pain relief was obtained in 36/52 patients with extensive pelvic side wall invoivement and swelling improved in 7/16. In Group II, Ir-192 was used in 6 patients and I-125 in 15. No postoperative deaths occurred. The overall median survival was 11 mo, with one patient surviving over 5 yr free of disease. Favorable prognostic factors for this type of treatment are an asymptomatic recurrence detected at routine examination, vaginal recurrences, and unilateral pelvic side wall involvement. Unfavorable factors include pelvic pain with leg edema, multiple sites of recurrence in the pelvis, and positive para aortic nodes. (11 Refs)

39. INTERSTITIAL IRRADIATION AS A SALVAGE TECHNIQUE.

Nisar Syed AM
Suite 217, 1245 Wilshire Blvd., Los Angeles, CA, 90017
Int J Radiat Oncol Biol Phys; 7(11):1613-1614 1981

Forty patients with recurrent pelvic malignancies were irradiated using temporary 192Ir and/or permanent 125I implants. All patients had been previously irradiated with 5,000-6,000 rad over 5-8 wk, and patients with cervical and vaginal carcinomas also had intracavitary irradiation (3,000-5,000 mg-hr). Overall local control was achieved in 27 patients: 13 remained alive after a minimum follow-up period of 2 yr. Palliation of other symptoms occurred in 80% of patients. Three patients developed enterovaginal and vesicovaginal fistulae. Interstitial irradiation provides palliation, local control, and a chance of cure in selected patients with recurrent pelvic malignancies. (9 Refs)

40. CYTOSOL ESTROGEN AND PROGESTERONE RECEPTORS IN NORMAL AND PATHOLOGICAL TISSUES OF THE HUMAN UTERUS AND OVARIES.

Baron J, Chwalisz K, Mikolajewska-Fischer Z, Adamski J
Klinika Endokrynologii Ginekologicznej, Instytut Ginekologii i Poloznictwa AM, ul. Polna 33, 60-535 Poznan, Poland
Ginekol Pol; 52(7):585-590 1981

Cytosol estrogen receptor (ER) and progesterone receptor (PR) levels were determined in normal and pathological tissues from endometria and ovaries. The samples were obtained from 30 women with normal endometrium, 20 women with normal myometrium, 10 women with normal ovaries, from 15 patients with endometrial carcinoma, 25 patients with uterine myoma, and 8 patients with ovarian neoplasms . The ER levels av (in femtomoles/mg) 193.4 in the follicular phase, 96.1 in the luteal phase, 166.7 in the climacterium (endometrium); 55.2 in the reproductive period and 49.3 in the climacterium in the myometrium, 22.1 in the normal ovaries, 160.6 in the patients with endometrial carcinoma (av age 62.2 yr), 104.5 in myoma (av age 43.9 yr), and 0-2,000 in ovarian neoplasms. The PR levels av 302.5 in the follicular phase, 125.2 in the luteal phase, 257 in the climacterium in the normal endometrium; 161.8 in the reproductive age and 121.4 in the climacterium in the normal myometrium; 67.1 in the normal ovaries; 131.5 (9-735) in endometrial carcinoma, 286 (0-705) in myoma, and 27-4,000 in ovarian neoplasms. The findings indicate the value of the determination of ER and PR levels in cytosol to evaluate the resistance of the target tissue to hormone therapy. (25 Refs) (In POL)

41. ROLE OF HORMONES INCLUDING DIETHYLSTILBESTROL (DES) IN THE PATHOGENESIS OF CERVICAL AND VAGINAL INTRAEPITHELIAL NEOPLASIA.

Robboy SJ, Truslow GY, Anton J, Richart RM
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Gynecol Oncol; 12(2,part2):S98-S110 1981

Current status of hormone usage and its relation to cervical neoplasia is reviewed. Analysis of neoplastic squamous cell lesions involving young women exposed prenatally to DES led to the definition of dysplasia and severe dysplasia and their separation from squamous dysplasia. Cytologic, histologic description, and correlation with DNA nuclear content are defined. Examination of DES-exposed women has shown discrepancies between cytology and biopsy specimens and possible intrinsic changes of the metaplastic and dysplastic cells. Comparison of rates of dysplasia in DES-exposed and nonexposed individuals within several yr will provide whether or not dysplasia occurs more frequently in DES-exposed women. Varied analysis of exposed and unexposed subjects disclosed that occurrence of dysplasia was more frequent in older subjects and in those who had intercourse with increased numbers of partners. Between the development of squamous cell carcinoma and DES exposure no link has been established. Recent studies have not resolved yet whether oral contraceptive agents play a causative role in the development of cervical neoplasia. Microglandular hyperplasia can also arise in young females exposed prenatally to DES. (48 Refs)

42. ASSOCIATION OF HUMAN PAPILLOMAVIRUS WITH NEOPLASTIC PROCESSES IN THE GENITAL TRACT OF FOUR WOMEN WITH IMPAIRED IMMUNITY.

Shokri-Tabibzadeh S, Koss LG, Molnar J, Romney S
(c/o Koss), Montefiore Hosp. and Medical Center, 111 East 210th St., Bronx, NY, 10467
Gynecol Oncol; 12(2,part2):S129-S140 1981

The presence of papillomavirus particles was documented by electron microscopy in atypical squamous epithelium of the cervix, vagina, and vulva, and in cells derived therefrom in f our women with compromised immune status who were being followed in our clinics. Three of the patients had treated Hodgkin's disease, and one a dermatologic disorder, perhaps akin to epidermodysplasia verruciformis. Initially, all four patients developed treatment-resistant condylomata acuminata of the vulva and adjacent areas. Subsequently one of the patients was shown to harbor in the vagina a focus of markedly atypical epithelium, perhaps a flat condyloma. Two other patients, followed for several years, developed multiple epidermoid carcinomas in situ affecting the cervix, vagina, and vulva. In one of these two latter patients the disease progressed to multiple foci of superficially invasive carcinoma. The possible role of the human papillomavirus in the genesis of these lesions is discussed. (Author abstract) (39 Refs)

SELECTED PRE-CLINICAL STUDIES

43. EXPERIMENTAL STUDIES OF CARCINOGENESIS OF THE UTERINE CERVIX IN MICE.

Wentz WB, Reagan JW, Fu YS, Heggie AD, Anthony DD
Dept. Reproductive Biology, Case Western Reserve Univ. Sch. Medicine, Cleveland, OH, 44106
Gynecol Oncol; 12(2,part2):S90-S97 1981

The histogenesis of cervical carcinomas induced in mice by coal-tar hydrocarbons or inactivated herpes simplex virus, Types 1 and 2, has been described. The lesions antedating the development of squamous cell carcinoma were similar to lesions encountered in patients with the same keratinizing type of carcinoma of the ectocervix. A theory for the development of the three grades of human cervical squamous cell carcinoma has been presented based on experimental and clinical data which demonstrate that each of the three grades of cancer consists of cells which resemble those of the tissue of origin and of the antecedent noninvasive lesion. (Author abstract) (20 Refs)

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VULVAR TUMORS

1. THE VALUE OF GROIN PALPATION IN EPIDERMOID CARCINOMA OF THE VULVA.

Iversen T

Norwegian Cancer Society, Dept. Gynecology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway

Gynecol Oncol; 12(3):291-295 1981

During the yr 1956-1974 258 patients with epidermoid carcinoma of the vulva were treated with radical vulvectomy and bilateral groin lymphadenectomy. Metastases to the superficial and/or deep inguinal lymph nodes were found in 100 cases (38.8%), only 64 of which were detected by clinical examination. In 40 more cases (15.5%) the groin lymph nodes were also suspected to be involved, but this could not be verified by microscopic examination. The 5-yr actuarial survival rate was 41% for the patients with lymph node metastases. There was a statistically significantly difference in the survival rate between the patients with palpable lymph node metastases as compared with those where the nodes were not suspected to be involved. (Author abstract) (9 Refs)

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2. ABDOMINOPELVIC COMPUTED TOMOGRAPHY IN THE PREOPERATIVE EVALUATION OF EARLY CERVICAL CANCER.

Grumbine FC, Rosenshein NB, Zerhouni EA, Siegelman SS
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Gynecol Oncol; 12(3):286-290 1981

The efficacy of abdominopelvic computed tomography (CT) in determining the extent of disease in the patient with early cervical cancer was evaluated in 24 patients (FIGO Stage Ia-1, Ib-18, IIa-5). The CT stage was compared to both the clinical and surgical pathological staging. CT was accurate only in 58% of the cases in determining parametrial extension. It was unable to detect any of the 6 cases of histologically documented lymph node metastases. CT appears to have limited use in the patient with early cervical carcinoma because with parametrial thickening it lacks sufficient specificity to differentiate between malignant and nonmalignant tissues and there is not sufficient sensitivity to detect early nodal involvement. (Author abstract) (24 Refs)

3. THE IMPACT OF LYMPH NODE STATUS ON SURVIVAL IN CERVICAL CARCINOMA.

Hammond JA, Herson J, Freedman RS, Hamberger AD, Wharton JT, Wallace S, Rutledge FN
Ontario Cancer Foundation, Victoria Hosp., 375 South St., London, Ontario, Canada
Int J Radiat Oncol Biol Phys; 7(12):1713-1718 1981

The relationship between results of lymphangiography (LAG) and other parameters and survival time was studied retrospectively in 215 patients with cervical carcinoma (CC) in Stages IB-IIIB. LAG results were classified as positive (LAG+) or negative (LAG-). All patients received external radiotherapy using a standard 15 x 15 cm pelvic field or, in patients with metastatic lymph nodes, an extended field. Internal radium implants were used when possible. Patients with large pelvic tumors who were LAG- were randomized to receive standard-field or extended-field external irradiation. Correlation of staging and LAG factors indicated three risk groups: good risk patients were Stage IIA or IIB and LAG- and av disease-free survival time (DFS) was greater than 92 Intermediate risk patients were Stage IIB and LAG+, or Stage IIIA or B and LAG-; av DFS was 31 mo. Poor risk patients were Stage IIIA or B and LAG+; av DFS was 11 mo. Among all three risk groups DFS was longer for those patients receiving radium implants. DFS was increased in LAG+ patients but not LAG- patients by the use of an extended radiation field. The 2-yr failure rate was 69.0% for LAG+ patients and 31.3% for LAG- patients. Persistent disease was found in 22.7% of LAG+ patients and 10.7% of LAG- patients. LAG status correlated with stage of disease. Results indicate that LAG is useful for defining high-risk patients with cervical carcinoma. (9 Refs)

4. HISTOLOGIC GRADE AND LYMPH NODE METASTASIS IN SQUAMOUS CELL CARCINOMA OF THE CERVIX.

Chung CK, Nahhas WA, Zaino R, Stryker JA, Mortel R
Div. Radiation Oncology, Dept. Radiology, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033
Gynecol Oncol; 12(3):348-354 1981

One hundred fifty-nine patients with squamous cell carcinoma of the cervix who underwent laparotomy were evaluated with regard to histologic grade, clinical stage, and surgical stage. Pelvic and/or paraaortic node metastases were also studied. Patients with poorly differentiated tumors, regardless of clinical stage, demonstrated pelvic and/or paraaortic nodal metastases more frequently than patients with better differentiated tumors. In patients with poorly differentiated tumors, staging discrepancies were more common. These findings suggest that histologic grading should be taken into consideration in the treatment planning of patients with cervical carcinoma. (Author abstract) (9 Refs)

5. CYTOPATHOLOGIC FEATURES OF GLASSY CELL CARCINOMA (MEETING ABSTRACT).

Pak HY, Paladugu RR, Yokota S, Agliozzo C
Division of Cytogenetics and Cytology, City of Hope National Medical Center, Duarte, CA, 91010
Am J Clin Pathol; 76(3):355 1981

Glassy cell carcinoma of the uterine cervix was initially described by Gluckmann and Cherry in 1956. In 1976, Littman and colleagues reported 13 additional cases claiming this tumor to be a distinct clinicopathologic entity which warranted a place in the classification of carcinoma of the cervix. They reported that this tumor did not have a distinctive cytologic appearance. All patients with carcinoma of uterine cervix treated at City of Hope National Medical Center since 1956 were reviewed; 16 show features of glassy cell carcinoma. Cytologic samples were evaluated in conjunction with histology. Characteristic cytomorphologic features of glassy cell carcinoma are finely granulated abundant cytoplasm with a large round or ovoid nucleus and a large nucleolus simulating atypical epithelial repair and regeneration as described by Giersson and associates. Emphasis is placed on cytological features to help in detecting this unusual variant of cervical carcinoma since the cytology of this lesion is not well recognized. (no Refs)

6. EA-ROSETTE TEST IN CERVICAL CELL SUSPENSIONS.

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AK St. Georg, Lohmuhlenstrasse 5, D-2000 Hamburg 1, W. Germany
Anal Quant Cytol; 3(4):281-284 1981

The erythrocyte-antibody (EA)-rosette test (RT), which detects constant fragment receptor-bearing cells within a cervical population, was studied as a potential screening technic for the early detection of cervical cancer. Of cervical suspensions from 2,437 patients, 54% had a negative RT: no EA-rosette-forming cells (ERFC) were observed. Forty-six percent had a positive RT test: one or more rosettes were observed. Comparison with conventional cytology showed that cytologically positive cases, containing severely dysplastic and carcinomatous cells, were 98.3% EA-rosette positive; only 1.7% were EA-rosette-negative. A cytologic preparation of ERFC from a cervical cell suspension is presented. The presence of ERFC cannot be predicted from the number of inflammatory cells seen in the conventional cytologic smear: cervical cell populations with numerous inflammatory cells may or may not contain ERFC. Three false negatives were reported, two in patients whose cytologic finding of severe dysplasia was confirmed histologically as carcinoma in situ. One patient with a false-negative RT had an invasive carcinoma that had been previously irradiated. Results suggest that the RT might decrease the necessity for cytologic screening and decrease the percentage of false-negative results in cytologic screening. (1 Ref)

7. CARCINOEMBRYONIC ANTIGEN IN CARCINOMA OF THE UTERINE CERVIX: ANTIGEN DISTRIBUTION IN PRIMARY AND METASTATIC TUMORS.

van Nagell JR, Hudson S, Gay EC, Donaldson ES, Hanson M, Powell DF, Goldenberg DM
Gynecologic Oncology, Univ. Kentucky Medical Center, 800 Rose St., Lexington, KY, 40506
Cancer; 49(2):379-383 1982

Immunohistochemical staining for carcinoembryonic antigen (CEA) was performed on primary tumors and regional lymph nodes from 100 patients undergoing radical hysterectomies and pelvic lymphadenectomies for invasive carcinoma of the uterine cervix. Antigen staining was present in 82% of keratinizing squamous carcinomas as compared with 50% in nonkeratinizing tumors. Seventeen patients with CEA-producing cervical cancer had regional lymph node metastases, all of which stained positively for CEA. Conversely, antigen could not be detected in lymph nodal metastases from primary tumors devoid of CEA. The pattern and intensity of CEA staining in primary tumors and their metastases were similar in all cases. Antigen was present in highest concentrations in the cytoplasm and tumor cell membrane of all tissues examined and isolated nuclear staining was absent. The clinical implications of these findings are discussed. (Author abstract) (21 Refs)

8. TREATMENT OF PREINVASIVE DISEASE OF THE CERVIX BY CONE BIOPSY.

Bevan JR, Attwood ME, Jordan JA, Lucas A, Newton JR
Inst. Obstetrics and Gynaecology, Queen Charlotte's Maternity Hosp., Goldhawk Road, London W6 0XG, England
Br J Obstet Gynaecol; 88(11):1140-1144 1981

During the yr 1952-1977, 646 patients with abnormal cervical cytology underwent cone biopsy (595) or ring biopsy of the cervix. The histological diagnoses were invasive carcinoma 20 (3%) microinvasive carcinoma 16 (2%), carcinoma in situ and severe dysplasia 418 (65%), other dysplasia 149 (23%). The remainder, 43 (7%) had no demonstrable abnormality. Following biopsy 41 (7%) patients with non-invasive disease had abnormal cytology within a yr of biopsy. A further 12 (2%) developed abnormal cytology after one yr. These recurrences occurred up to 12 yr after the initial treatment, and in one patient invasive squamous carcinoma has developed. (Author abstract) (18 Refs)

9. CARCINOMA IN SITU OF THE CERVIX IN THE POSTMENOPAUSAL FEMALE.

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Int J Gynaecol Obstet; 19(6):491-494 1981

Of 178 patients with carcinoma in situ of the cervix, 11 were postmenopausal (44-83 yr old). Initial cytological examination showed squamous cell carcinoma in seven patients, marked atypia in two, and mild atypia in two. Colposcopic examination was carried out in 7/11 patients: the most common finding was a white lesion associated with prominent vascular pattern. Histological examination of cervical biopsy specimens showed carcinoma in situ in 9/11 patients and atypia in 1; 1 had negative biopsy. Surgery was performed in all 11 patients: 3 underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, 6 underwent conization and hysterectomy, 1 patient with a history of subtotal hysterectomy underwent cervicectomy, and 1 underwent conization. At follow-up examination, 10 patients had no evidence of recurrence and 1 developed recurrence in the apex of the vagina 3 yr after total hysterectomy. (4 Refs)

10. PRETREATMENT LAPAROTOMY IN CARCINOMA OF THE CERVIX.

Welander CE, Pierce VK, Nori D, Hilaris BS, Kosloff C, Clark DG, Jones WB, Kim WS, Lewis JL
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Gynecol Oncol; 12(3):336-347 1981

In cases of advanced carcinoma of the uterine cervix, control of regional pelvic disease is not always equated with survival. While early disease often does remain localized within the pelvis, more advanced cervical cancers are observed to metastasize to paraaortic nodes and to distant sites. This study reports a surgical protocol designed to define extent of disease in patients having invasive cervical carcinoma prior to administering primary radiation therapy. Three questions have been raised: (1) Which individual patients have disease outside the pelvis? (2) Is it possible to modify therapy to control disease outside the pelvis and thereby influence survival? (3) Are positive paraaortic nodes found at pretreatment laparotomy indicative of systemic spread of disease? This pretreatment laparotomy was done on 127 patients, 31 of whom were found to have positive paraaortic nodes (24.4%). Sixteen patients had metastatic disea se within the peritoneal cavity. Standard pelvic radiotherapy was subsequently given, supplemented with a paraaortic field in those cases with positive paraaortic nodes. Survival was not significantly different in patients with or without paraaortic nodal disease. It was further noted that 17 of the 31 patients (54.8%) who had positive paraaortic nodes later had distant metastases (median time 8 mo), compared to 24/96 (25.0%) with negative nodes having a median time to metastases of 10 mo. (Author abstract) (11 Refs)

11. PRELIMINARY REPORT OF THE M.D. ANDERSON HOSPITAL RANDOMIZED TRIAL OF NEUTRON AND PHOTON IRRADIATION FOR LOCALLY ADVANCED CARCINOMA OF THE UTERINE CERVIX.

Morales P, Hussey DH, Maor MH, Hamberger AD, Fletcher GH, Wharton JT
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Int J Radiat Oncol Biol Phys; 7(11):1533-1540 1981

Between February 1977 and August 1979, 75 patients with locally advanced carcinoma of the uterine cervix were randomized to receive mixed beam or photon irradiation. All patients were evaluated in the fifth wk for completion of treatment with intracavitary irradiation or an external beam boost using randomized modality. Local tumor control, complications, and patient survival were reviewed. There were 43 patients in the mixed beam group (combination of 50-mega electron volt (MeV) neutrons and 25-MeV photons +- intracavitary radium), and 32 in the photon group (25-MeV photons +- intracavitary radium). Seventy-one patients had previously untreated squamous carcinoma of the cervix, one had adenocarcinoma of the cervix, and three had squamous carcinoma recurrent following radical hysterectomy. Approx one-fourth of the patients in each group had clinical evidence of pelvic lymph node metastasis. External beam treatments were delivered 5x/wk using 200-rad fractions. Mixed beam treatments were given 3x/wk with photons and 2x/wk with neutrons (65 rad, equivalent to 200 rad with photons). Two portal arrangements were used for total pelvis irradiation with photons: a two-field technique and a four-field box technique. There was no difference between the mixed beam and photon groups with respect to local control, frequency of complications, and patient survival. Results achieved with photons were superior to those achieved

with mixed beam irradiation for Stage IIIA tumors. Major complications occurred in four patients of the mixed beam group and two of the photon group. Better results were obtained in patients who completed treatment with intracavitary radium. The local control rate with mixed beam irradiation plus intracavitary radium was 81% as compared with 65% for the photon plus intracavitary radium group, although this difference was not statistically significant. (7 Refs)

12. RADIATION-INDUCED TUMOR REGRESSION AS A PROGNOSTIC FACTOR IN PATIENTS WITH INVASIVE CERVICAL CANCER.

Hardt N, Van Nagell JR, Hanson M, Donaldson E, Yoneda J, Maruyama Y
(c/o van Nagell), Div. Gynecologic Oncology, Univ. Kentucky, Lexington, KY, 40536
Cancer; 49(1):35-39 1982

Radiation-induced tumor regression was evaluated as a prognostic factor in 200 patients with invasive cervical cancer treated at the University of Kentucky Medical Center during the yr 1973-1977. Radiation responses were classified as complete (Type A), intermediate (Type B), or incomplete (Type C) based upon pelvic examination findings 1 mo following completion of therapy. Patients with Type A response to radiation had a recurrence rate of 5%, as compared with 27% in patients with a Type B response and 85% in patients with a Type C response. The direct relationship between radiation response and the incidence of tumor recurrence was observed in all stages of disease. Seventy-five percent of patients with Stage IB and IIB disease and a Type C response to radiation developed recurrent cancer, and tumor recurrences were confined to the central pelvis in the majority of cases. Patients with keratinizing squamous cell cancers had the lowest incidence of complete response to radiation. These findings suggest that careful observation of cervical cancer throughout radiation therapy can provide prognostically significant information concerning radiation-induced tumor regression. The therapeutic implications of this data are discussed. (Author abstract) (22 Refs)

13. PROGNOSTIC SIGNIFICANCE OF PERITONEAL CYTOLOGY IN PATIENTS WITH ENDOMETRIAL CANCER AND PRELIMINARY DATA CONCERNING THERAPY WITH INTRAPERITONEAL RADIOPHARMACEUTICALS.

Creasman WT, Disaia PJ, Blessing J, Wilkinson RH, Johnston W, Weed JC
Dept. Obstetrics and Gynecology, Duke Univ. Medical Center, Durham, NC, 27710
Am J Obstet Gynecol; 141(8):921-929 1981

One hundred sixty-seven patients with clinical Stage I carcinoma of the endometrium were treated primarily by operation consisting of total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, and cytologic testing of peritoneal washings. Twenty-six (15.5%) of the 167 patients had malignant cells identified on cytologic examinations of peritoneal washings. Recurrence developed in 10 of these 26 (34.0%) compared to 14/141 (9.9%) patients with negative cytologic testing. Of the 26 patients, 13 (50%) had disease outside of the uterus at operation and seven had died of disease (54%). Thirteen patients had malignant cells in the peritoneal washings but no disease outside of the uterus and 6 (46%) of these have died of disseminated intra-abdominal carcinomatosis. On the basis of the poor outcome of those patients who had malignant cells in the peritoneal washings in the 167 patients studied, a plan of treating such patients with intraperitoneal radioactive chromic phosphate suspension (P-32) was instituted. Twenty-three subsequent patients with clinical Stage I carcinoma of the endometrium were found to have malignant cells in the peritoneal fluid. All 23 received intra-abdominal P-32 suspension instillation after operation. There have been three recurrences with two patients dying of disease. All of the three recurrences appeared at sites distant from the abdominal cavity. Peritoneal cytologic examination appears to be an important factor in the prognosis of endometrial cancer and, when the washings are positive for malignant cells, intraperitoneal chronic phosphate therapy appears to be efficacious. (Author abstract) (10 Refs)

14. INVASIVE SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX. III. A MALIGNANCY GRADING SYSTEM FOR INDICATION OF PROGNOSIS AFTER RADIATION THERAPY.

Stendahl U, Eklund G, Willen H, Willen R
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Acta Radiol Oncol Radiat Phys Biol; 20(4):231-243 1981

The predictive value of a malignancy grading system embodied by eight histopathologic parameters and of staging, age, yr of admission and the different treatment modalities were compared in relation to 5-and 8-yr survival. The material consisted of 196 patients in Stage II according to the FIGO classification. The grading system proved superior with high significance (p less than 0.001) to the other predictors including each histopathologic parameter apart from vascular invasion (p = 0.01). All histopathologic parameters but two (differentiation into cell type and mitosis) exhibited a significant (p less than 0.01) decrease in survival with higher grade at the 5-and 8-yr controls. Patients in Stage II could be divided into groups with low, intermediate and high malignancy points. Both groups of extremes showed a marked and highly significant difference in survival rates compared with the intermediate group, and the grading system made it possible to predict 60% of the patients with acceptable specificity. In the group of high malignant tumors the system maintained a continual prognostic value even among patients still alive at the 5-yr control. (Author abstract) (50 Refs)

15. ADENOCARCINOMA OF THE UTERINE CERVIX.

Berek JS, Castaldo TW, Hacker NF, Petrilli ES, Lagasse LD, Moore JG
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. California Los Angeles Sch. Medicine, Los Angeles, Ca, 90024
Cancer; 48(12):2734-2741 1981

One hundred patients with primary adenocarcinoma of the uterine cervix were evaluated. Of the 48 Stage I patients, 13 were treated with radical surgery, 16 with radiation alone, and 19 with combination therapy. Life table analysis of Stage I patients showed no significant difference in survival for those treated with radical surgery or combination therapy. Both groups had a greater 5-year survival (p less than 0.05) than those treated with radiation. Recurrences in Stage I were more frequent with primary radiation alone, both locally and at distant sites (p less than 0.01). Greater tumor size was related to poorer survival, and failures in patients with larger lesions were more common in those treated with radiation therapy. Survival for the 32 Stage II patients was greater for those treated with combination therapy. Higher tumor grade was associated with poorer survival for each stage, regardless of treatment. More complications were associated with radiation

therapy than with radical surgery. Radiation therapy alone is not sufficient for patients with Stage I and II disease, and radical surgery may be appropriate treatment for Stage I disease. (Author abstract) (21 Refs)

16. SEQUENTIAL COMBINATION OF BLEOMYCIN AND MITOMYCIN IN ADVANCED CERVICAL CANCER - AN AMERICAN EXPERIENCE: A NORTHERN CALIFORNIA ONCOLOGY GROUP STUDY.

Greenberg BR, Hannigan J, Gerretson L, Turbow MM, Friedman MA, Hendrickson CA, Glassberg A, Carter SK
Section Hematology and Oncology, Univ. California, Davis, Medical Center, 4301 X St.-FOLB-11-B, Sacramento, CA, 95817
Cancer Treat Rep; 66(1):163-165 1982

Eighteen evaluable patients with advanced squamous cell carcinoma of the cervix were treated with a sequential combination of bleomycin and mitomycin. We observed no complete responses and only four partial responses (22% response frequency). The median duration of response was only 3.4 mo, and the median survival time for the partial responders was 8.5 mo vs 4.0 mo for the nonresponders. Three cases of bleomycin pulmonary toxicity were reported, two of a severe grade. It appears that this combination is of limited effectiveness and is inferior to other combinations. (Author abstract) (6 Refs)

17. RETINOIDS AND THE PREVENTION OF CERVICAL DYSPLASIAS.

Romney SL, Palan PR, Duttagupta C, Wassertheil-Smoller S, Wylie J, Miller G, Slagle NS, Lucido D
Dept. Gynecology/Obstetrics, Albert Einstein Coll. Medicine, 1300 Morris Park Ave., Bronx, NY, 10461
Am J Obstet Gynecol; 141(8):890-894 1981

Women with abnormal cytology were matched with normal control subjects for age, parity, ethnicity, and socioeconomic class and participated in a blind case-control study focused on the role of nutrition in cervical dysplasia. Sucrose gradient ultracentrifugation studies for determination of the presence and concentration of the binding proteins for retinol and retinoic acid were performed on colposcopic biopsy tissue specimens. The nutritional survey revealed statistically significant differences for vitamins A and C and beta carotene. Retinol binding protein was absent or minimally detectable an d inversely related to the severity of the dysplasia. It is proposed that a double-blind clinical trial be conducted to evaluate whether retinoids may pharmacologically inhibit, arrest, or reverse cervical dysplasia. (Author abstract) (16 Refs)

18. LYMPH NODE POSITIVITY IN CERVICAL CANCER.

Heller PB, Lee RB, Leman MH, Park RC
Gynecologic Oncology Service, Dept. Obstetrics and Gynecology, Walter Reed Army Medical Center, Washington, DC, 20012
Gynecol Oncol; 12(3):328-335 1981

From January 1962 until July 1978, 44 patients with invasive cervical cancer at exploratory surgery were found to have positive lymph nodes. Forty-three of these patients received radiation as definitive therapy after the discovery of lymph node metastasis. One patient had a positive left scalene biopsy as well and was treated only with chemotherapy. Thirty-three of the patients were clinically Stage IB. Two patients were Stage IIA, while seven were IIB. There was one individual staged as IIIB. One patient was unstageable because of carcinoma found at operation for benign disease. Histologically, 35 of the 44 had squamous cell carcinoma. Five patients had adenocarcinoma, while two were adenosquamous. One patient was noted to be glassy cell type, and one patient had small cell undifferentiated carcinoma. Evaluation of the 44 operative specimens comparing clinical stage to highest positive node revealed that 32 patients (73%) had external iliac/obturator node involvement. Twenty-five of these were clinically Stage I disease. Twelve patients (27%) had involvement above the external iliac/obturator level and 8 of these were clinically Stage I. It is evident that a number of patients who are thought to have early disease clinically may have more advanced disease surgically and pathologically. Using the actuarial method of Berkson and Gage, the 5-yr survival rate of the entire 44 operated patients was 52%. For comparison with other studies, we have additionally divided the patients into: (1) 22 who had completed hysterectomies and lymph node dissections followed by radiotherapy; (2) 22 who had lymph node sampling followed by radiation or chemotherapy alone. The actuarial survival of the first group was 71%. The survival of the second group, which included clinical Stages I, II, and III and one unstageable patient, was 34%. (Author abstract) (11 Refs)

19. HUMAN PAPILLOMAVIRUS (HPV) IN CONDYLOMATOUS LESIONS OF CERVIX: A COMPARATIVE ULTRASTRUCTURAL AND IMMUNOHISTOCHEMICAL STUDY.

Ferenczy A, Braun L, Shah KV
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Am J Surg Pathol; 5(7):661-670 1981

Cervical condylomata classified histologically as flat, papillary, or endophytic were obtained from 97 patients (16-35 yr old). Transmission electron microscopy (TEM) was used to dete ct the presence of human papillomavirus (HPV) particles; the immunoperoxidase technique (IPT) was used to detect viral antigen. HPV particles were found in 24/97 specimen by TEM. Viral particles were demonstrated in 21/68 flat and 3/26 papillary condylomata. Viral antigen was found in 47/97 specimens by IPT. All specimens positive by TEM were also positive by IPT, confirming the specificity of the immunological staining. The viral antigen was detected in 38/68 specimens of flat condylomata, in 9/26 papillary condylomata, and in 0/3 endophytic condylomata. Prevalence of HPV correlated with the extent of koilocytosis rather than with histiotype. IPT is of value for further characterizing cervical condylomata and the relationship between HPV infection and cervical intraepithelial neoplasia. (23 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

20. USE OF THE COMPUTED TOMOGRAPHIC WHOLE BODY SCANNER TO STAGE AND FOLLOW PATIENTS WITH ADVANCED OVARIAN CARCINOMA.

Whitley N, Brenner D, Francis A, Kwon T, Villasanta U, Aisner J, Wiernik P, Whitley J
Dept. Radiology, Univ. Maryland Hosp., Baltimore, MD, 21201
Invest Radiol; 16(6):479-486 1981

Advanced ovarian carcinoma continues to be a difficult tumor to evaluate noninvasively. Recent developments in chemotherapy have enhanced response rates in this disease, thus improving the likelihood of tumor regression. Computed Tomography (CT) allows the noninvasive estimation of tumor extent in patients with ovarian carcinoma. Seventeen patients

with epithelial ovarian carcinoma had 22 whole body CT scans performed either just prior to or following laparotomy. For determination of tumor involvement, when the CT was positive, a high pathologic correlation was found at liver, ascitic, peritoneal, mesenteric, and omental sites (sensitivity). When the CT was negative, high pathologic correlation was found at ascitic and mesenteric sites (specificity). Lower and negative correlation at other disease sites is attributed to difficulty of CT detection of small (1 cm) tumor nodules on visceral surfaces. Eighteen patients with advanced ovarian carcinoma were followed prospectively during treatment with repetitive CT scans. CT results were compared with physical examination, other radiologic studies, and clinical status. In 83% (15/18) of patients and 88% (59/67) of CT scans performed, CT was found to contribute useful management information. Clinical decisions were made on the basis of CT alone in 43% (29/67) of scans performed. These data suggest that CT scanning is very useful in the staging and follow-up of patients with ovarian carcinoma and can replace other radiologic procedures, but it is not completely accurate and needs to be correlated with physical examination and in cases without tumors visible with CT, with laparotomy. (Author abstract) (14 Refs)

21. GRANULOSA-THECA CELL TUMORS IN PREMENARCHAL GIRLS. A CLINICAL AND PATHOLOGIC STUDY OF TEN CASES (MEETING ABSTRACT).

Lack EE, Perez-Atayde AR, Goldstein DP, Crigler JF, Vawter GF
Department of Pathology, Children's Hospital Medical Center, Boston, MA, 02115
Am J Clin Pathol; 76(3):353 1981

Granulosa-theca cell tumors (GTCT) in the premenarch accounted for 4% of childhood ovarian tumors treated from 1928 through 1979. The av age of the ten girls at diagnosis was 5 yr (range 11 mo to 12 1/2 yr) and precocious 'pseudopuberty' was the most common presentation. GTCT were solitary (five right, five left) with an av diameter of 12.1 cm. Histology showed a diffuse or macrofollicular pattern with prominent luteinization; Call-Exner bodies and folded ('coffee bean') nuclei were inconspicuous. Ultrastructure showed abundant smooth endoplasmic reticulum and mitochondria with tubulo-vesicular cristae; prolactin, estradiol and testosterone were detected in one GTCT using immunologic technics. The av follow-up was 21 yr; nine girls were followed in excess of ten yr. Salpingo-oophorectomy was curative despite tumor spillage in two. Invasive breast cancer occurred in two long-term survivors. The prognosis of these GTCT appears favorable but further study is needed to completely define their biologic potential; the possible association with subsequent breast cancer merits further investigation as well. (no Refs)

22. OVARIAN CARCINOMA: HISTOLOGIC AND CLINICAL CORRELATION OF CYTOPLASMIC ESTROGEN AND PROGESTERONE BINDING.

Creasman WT, Sasso RA, Weed JC, McCarty KS
Div. Oncology, Duke Univ. Medical Center, Durham, NC, 27710
Gynecol Oncol; 12(3):319-327 1981

Primary ovarian carcinomas from 18 patients, ages 27-79, were evaluated for the presence of estrogen- and progesterone-binding proteins. The levels of cytosolic sex steroid receptor were compared to histology, nuclear grade, and the patients' clinical course. The data suggest that nuclear grade and receptor status each correlate with the patients' clinical course. The simultaneous presence of both estrogen and progesterone receptor proteins tend to be noted in tumors with more well-differentiated nuclei. It is suggested that the determination of biochemical cytosolic receptor status may become an important addition to tumor type, nuclear grade, and staging as prognostic indicators in patients with ovarian carcinoma. Histochemical staining for estrogen-binding localization did not correlate with SDGA and DCCA receptor analysis nor with clinical parameters. (Author abstract) (31 Refs)

23. BETA-HEXOSAMINIDASE ACTIVITIES AND ISOENZYMES IN NORMAL HUMAN OVARY AND OVARIAN ADENOCARCINOMA.

Chatterjee SK, Chowdhury K, Bhattacharya M, Barlow JJ
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Cancer; 49(1):128-135 1982

Levels and isoenzyme profiles of beta-hexosaminidase were compared in extracts from normal ovaries and ovarian epithelial tumors. The specific activities of beta-hexosaminidase were significantly (p less than 0.001) higher in malignant than in normal ovarian tissues. The enzyme levels of the tumors depended on their degree of differentiation. Well-differentiated tumors had activities in the normal range, while poorly differentiated ones had values higher than the normal mean + 2 SD. The moderately and moderately to poorly differentiated tumors had intermediate levels. DEAE-cellulose chromatography was used to resolve the isoenzymes of beta-hexosaminidase. Two major forms, beta-hexosaminidase A and beta-hexosaminidase B, were detected in all the preparations. In one tumor specimen, a component eluting slightly ahead of beta-hexosaminidase A was also detected. For quick separation, a batch-wise procedure using DEAE-cellulose was adapted. Proportions of the isoenzymes A and B separated by batch-wise procedure were similar to those obtained by column chromatography. Heat stability, optimum pH, acid stability and substrate specificity of the beta-hexosaminidase isoenzymes from ovarian tissues were similar to those from other human sources. Isoenzymes from tumor extracts were more labile to heat and acid pH compared with those from normal source. Slight differences in the affinity for the substrate p-nitro-phenyl-beta-N-acetyl-galactosaminide between the isoenzymes from normal and malignant ovaries were noted (Author abstract) (28 Refs)

24. NEUROHORMONAL PEPTIDES IN OVARIAN CARCINOIDS: AN IMMUNOHISTOCHEMICAL STUDY OF 81 PRIMARY CARCINOIDS AND OF INTRAOVARIAN METASTASES FROM SIX MID-GUT CARCINOIDS.

Sporrong B, Falkmer S, Robboy SJ, Alumets J, Hakanson R, Ljungberg O, Sundler F
Dept. Obstetrics and Gynecology, Malmo General Hosp., S-214 01 Malmo, Sweden
Cancer; 49(1):68-74 1982

Eighty-one primary ovarian carcinoids and intraovarian metastases from six mid-gut carcinoids were examined for the presence of tumor cells immunoreactive with antisera raised against various neurohormonal peptides, mostly of gastroenteropancreatic (GEP) origin. Twenty of the primary and two of the metastastic carcinoids contained such tumor cells. The incidence of tumors with any kind of neurohormonal peptide immunoreactive tumor cells was 53% in the trabecular carcinoids, and 42% in the strumal carcinoids, whereas the incidence was much lower (7%) in the insular type. Immunoreactive pancreatic polypeptide (PP), glucagon, enkephalin, and somatostatin were those neurohormonal peptides most commonly observed in the tumor cells of the primary carcinoids.

Those less commonly found were substance P, calcitonin, VIP, neurotensin, beta-endorphin, and ACTH. Four metastatic carcinoids were nonreactive with all the antisera used. Ce lls storing inmunoreactive insulin, glucagon, PP, VIP, gastrin, substance P, or enkephalin were found in one of the two remaining metastatic carcinoids; in the other oniy gastrin-immunoreactive tumor cells were observed. The occurrence and distribution of tumor cells storing the neurohormonal peptides in ovarian carcinoids are discussed in relation to their possible origin in the ovary and to carcinoids in the gut. (Author abstract) (32 Refs)

25. INDICATIONS AND THERAPEUTIC RESULTS WITH INTRAPERITONEAL COLLOID ISOTOPE TREATMENT OF OVARIAN TUMORS.

Keller G, Kuhn E, Krommer K
Radiologiai Klinika, Pecsi Orvostudomanyi Egyetem, Pecs, Hungary
Magy Onkol; 25(4):240-246 1981

One hundred and eighty-six patients with ovarian tumors were subjected to ip colloid isotope treatment (198Au: 180-200 Mci, or 111Ag: 45-55 mCi) 2-4 wk after surgery (mostly complete tumor resection, with or without hysterectomy and adnexectomy). Proliferating serous-mucinous cysts were diagnosed in 22 patients (Group 1b-2b), papillary cystic carcinoma in 50 (Group 1c), mucinous cystic carcinoma in 45 (Group 2c), endometrioid adenocarcinoma in 27 (Group 3c), anaplastic carcinoma in 14 (Group 4c), embryonal teratoma in 4 (Group 4), and granulosa-cell tumor in 24 (Group 6). Stage I was established in 112 patients, Stage II in 48, Stage III in 22, and Stage IV in 4. The 3-and 5-yr symptom-free survival rates were 16/16 and 14/15, respectively, in Group 1b-2b; 73.3% and 63.1% in Group 1c; 70.6% and 60.6% in Group 2c, 42.3% and 36.4% in 3c, 4/14 and 1/14 in 4c, and 85% and 82.3% in Group 6. In Groups 1c, 2c and 3c combined, the 3-yr symptom-free survival rates were 62% after complete tumor removal and 36% after partial resection. (34 Refs) (In HUN)

26. LONG TERM CHEMOTHERAPY WITH FT-207 FOR OVARIAN CARCINOMA.

Sugimori H, Tanaka M, Jimi S, Watanabe E, Kato Y, Morita T, Shigyo R, Yamashita H, Nishimura A, Kawakami M, Toyota Y, Tsukamoto N, Matsuyama T, Taki I
Dept. Obstetrics and Gynecology, Saga Medical Sch., Saga, Japan
Nippon Gan Chiryo Gakkai Shi; 16(4):633-640 1981

5-fluoro-1-(tetrahydro-2-furyl)-uracil (FT-207) was administered as maintenance therapy to 69 patients (14-78 yr old) with ovarian cancer. The patients had been initially treated with surgery (31 complete resection, 38 incomplete resection), radiotherapy (32), and other chemotherapy (46) to induce regression of the tumors. According to staging criteria for adenocarcinomas, 21 cases were Stage I, 9 were Stage II, 22 were Stage III, 2 were Stage IV, and 6 were recurrent tumors. FT-207 was administered 400-1,600 mg/day for 3-6 mo to 35 patients, 6-12 mo to 17, up to 2 yr to 8, or greater than 2 yr to 4 patients. Administration of FT-207 was discontinued because of side effects (8 cases), ineffectiveness (18), patient's wishes (2), or other reasons (2). Primary side effects included gastrointestinal problems (13 cases), general malaise (8), skin disease (4), leukopenia (4), hepatic obstruction (2), and headache (1). According to FT-207 dosage, 0/3 patients were given 400 mg/day, 5/23 had 600 mg/day, 9/30 were given 800 mg/day, 5/6 had 1,200 mg/day, and 2/3 were given 1,600 mg/day. All patients experienced side effects. Compared to control patients who recieved FT-207 alone, the patients given the FT-207 in combination with other modalities had an effective form of treatment for ovarian cancer. (12 Refs) (In JPN)

27. HIGH-DOSE MEDROXYPROGESTERONE ACETATE (MPA) IN ADVANCED EPITHELIAL OVARIAN CANCER RESISTANT TO FIRST- OR SECOND-LINE CHEMOTHERAPY.

Mangioni C, Franceschi S, La Vecchia C, D'Incalci M
(c/o D'Incalci), Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62-20157 Milan, Italy
Gynecol Oncol; 12(3):314-318 1981

Out of 33 evaluable patients with advanced ovarian cancer, resistant to extensive polychemotherapy, then treated with high-dose im medroxyprogesterone (MPA), five partial responses (15%) were obtained. No partial response was obtained in a comparable group of 30 patients treated with an oral schedule. Four patients (2 po, 2 im) had stable disease for at least 3 mo, and 16 experienced subjective improvement. Treatment was very well tolerated. This study shows that high-dose MPA has some activity in ovarian cancer, and is worthy of further investigation. (Author abstract) (7 Refs)

28. CHEMOTHERAPY OF OVARIAN CANCER DIRECTED BY THE HUMAN TUMOR STEM CELL ASSAY.

Alberts DS, Chen HS, Salmon SE, Surwit EA, Young L, Moon TE, Meyskens FL
Section Hematology/Oncology, Coll. Medicine, Univ. Arizona, Tucson, AZ, 85724
Cancer Chemother Pharmacol; 6(3):279-285 1981

The human tumor stem cell assay (HTSCA) was used to study the in vitro sensitivity rates of anticancer drugs used in the treatment of 115 patients with previously untreated and relapsing ovarian cancer. The data have identified patterns of cross resistance and residual sensitivity between anticancer drugs and have allowed the prospective selection of single agents possessing in vitro activity for the treatment of 32 patients with relapsing disease. The most active agents in vitro against ovarian tumor colony forming units from previously untreated and relapsing patients were cis-platinum and vinblastine. Evidence for in vitro cross resistance between melphalan and adriamycin, and between melphalan and bleomycin was found in the previously untreated patients. In 11 of the 32 patients, in vitro testing predicted sensitivity to single agents: 8 of the patients had partial remission lasting a median of 3.3 mo. In 33 instances HTSCA had 100% accuracy in predicting the lack of clinical response. HTSCA for advanced ovarian cancer appe ars to have a similar predictive accuracy rate to the estrogen receptor assay for predicting the response to hormonal therapy for disseminated breast cancer. (28 Refs)

29. EPITHELIAL CARCINOMA OF THE OVARY.

Morales PH, Fayos JV
(c/o Fayos) Div. Radiotherapy, Dept. Radiology, Univ. Miami Sch. Medicine, P.O. Box 016960, Miami, FL, 33101
Int J Radiat Oncol Biol Phys; 7(12):1649-1654 1981

Results of treatment of 176 cases of epithelial carcinoma of the ovary are reported. Patients had a mean age of 52 yr (range 16-81 yr). Histological types included serous (59%), mucinous (7.4%), endometrioid (11.4%), mesonephric (6.3%), and 'other carcinomas' (15.8%). Staging indicated 33% of patients were Stage I, 24% Stage II, 38.6% Stage III, 3.4% Stage IV, and 1% unclassified. Surgical treatment included total hysterectomy and bilateral salpingo-oophorectomy in 99 cases and more limited surgery in the other cases (diagnostic biopsy alone in 14 cases and partial or total omentectomy in 37 cases). Irradiation (5,000 rads) was administered to the pelvis alone or to the pelvis and part of the abdomen, depending on the extent

of disease. Patients with advanced disease received post-irradiation chemotherapy with chlorambucil (CA). Pre- and post-irradiation CA was given to 26 patients. Five-yr survival rates were 42% overall, 77% for Stage I, 31% for Stage II, 23% for Stage III, and 0% for Stage IV. Fifteen-yr survival rates (15SR) were 72% for Stage I, 27% for Stage II, and 18% for Stage III. Patients in whom tumor resection was complete showed 59% 15SR compared with 20% for those with incomplete resection. Secondary malignancies were found in 20% of patients either during initial surgery or at other times. Autopsy findings showed uncontrolled pelvic and/or abdominal disease in 25/25 cases. (21 Refs)

30. SMALL CELL CARCINOMA OF THE OVARY WITH HYPERCALCEMIA: A REPORT OF ELEVEN CASES.

Dickersin GR, Kline IW, Scully RE
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Cancer; 49(1):188-197 1982

Eleven cases of a small cell ovarian cancer associated with hypercalcemia that was reversed by removal of the tumor are reported and compared with three similar cases in the literature. The 14 cases account for 50% of recorded cases of ovarian-cancer-related hypercalcemia. The 14 tumors occurred in women between the ages of 13 and 35, with an av of 22 yr and, with two exceptions, behaved clinically in an aggressive fashion. Light and electron microscopic study confirmed the epithelial nature of the neoplasms but failed to disclose their specific subtype or origin. (Author abstract) (26 Refs)

31. PRIMARY OVARIAN MALIGNANT MELANOMA ARISING IN CYSTIC TERATOMA.

Cronje HS, Woodruff JD
Dept. Gynecological Pathology, Johns Hopkins Hosp., Sch. Medicine, Baltimore, MD , 21205
Gynecol Oncol; 12(3):379-383 1981

Primary malignant melanoma of the ovary is a rare neoplasm. This report describes the seventh well-documented case arising in the ovary of a 74-yr-old white widow. A unilateral ovarian teratoma was removed, within which was found a malignant melanoma. Junctional activity of melanocytes was demonstrated in the epidermis within the teratoma. An extraovarian primary melanoma was not recognized. The patient was treated with a unilateral salpingo-oophorectomy. She died 2 1/2 yr later of bone metastases from the melanoma, confirmed at autopsy. This case is described and the literature reviewed. (Author abstract) (19 Refs)

32. NONCONTRACEPTIVE ESTROGEN USE AND THE OCCURRENCE OF OVARIAN CANCER.

Weiss NS, Lyon JL, Krishnamurthy S, Dietert SE, Liff JM, Daling JR
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
JNCI; 68(1):95-98 1982

Female residents of six counties in Washington and Utah in whom ovarian cancer was diagnosed during 1975-79 were interviewed concerning prior use of noncontraceptive estrogens. Interviews with a random sample of women drawn from these counties were obtained for comparison. Taken as a whole, women with epithelial ovarian tumors reported estrogen use for 1 yr or more somewhat more often than did controls [relative risk (RR) = 1.3, 95% confidence interval (CI) = 0.9-1.8]. The proportion of women who had used estrogens varied according to the histology of their tumor, notably, of 17 women with endometrioid tumors, 12 had used estrogens (RR = 3.1, 95% CI = 1.0-9.8). the excess risk of endometrioid carcinoma related to estrogen use was not further increased when these hormones were taken for long durations, in high doses, or proximate to the time of diagnosis. Neither was there any evidence of increased risk from estrogen use in the small group of women with clear cell tumors, a histologic tumor type believed to be closely related to endometrioid carcinoma. Thus the observed association between menopausal estrogen use and the occurrence of ovarian endometrioid tumors should be interpreted cautiously until the results of additional studies are available. (Author abstract) (19 Refs)

33. OVARIAN EPITHELIAL CANCER AND CHEMICAL CARCINOGENESIS.

Venter PF
Dept. Obstretrics and Gynecology, Univ. Orange Free State, Bloemfontein, South Africa
Gynecol Oncol; 12(3):281-285 1981

Ovarian cancer is the most common fatal gynecological malignancy and is on the increase in industrialized countries. At this moment it is almost impossible to identify the high-risk patient. This cancer could be initiated by a chemical carcinogen via the vagina, uterus, and tubes and the substance promoting the cancer could be steroid-rich antral fluid from ruptured follicles. There is ample clini cal evidence available for migration of chemical substances from the vagina to the peritoneal cavity and ovaries. By use of the radionuclide 99mTc-HAM upward migration was also demonstrated. Many different chemical substances are regularly used in the vulvo-vaginal areas and some of these could be implicated in carcinogenesis. (Author abstract) (31 Refs)

TROPHOBLASTIC DISEASE

34. ROENTGENOLOGIC MANIFESTATIONS OF PULMONARY METASTASES IN CHORIOCARCINOMA AND INVASIVE MOLE.

Sung HC, Wu PC, Hu MH, Su HT
Dept. Obstetrics and Gynecology, Capital Hosp., Peking, People's Republic of China
Am J Obstet Gynecol; 142(1):89-97 1982

From 1949 to 1975, a total of 3,915 chest films were taken for 429 cases of choriocarcinoma and 441 cases of invasive mole. The incidences of pulmonary metastases were 85.1% and 65.0%, respectively. The various forms of pulmonary metastases were studied and correlated with clinical symptoms and pathologic changes. In order to follow up the progression or regression of the various forms, serial chest films were taken at intervals of 10 to 14 days in 27 cases. In eight cases postmortem pulmonary arteriograms were obtained on the autopsied lung specimens for the study of vascular changes of metastatic lesions. Pathologic examinations and pulmonary arteriography were also done on the surgically resected lung specimens. As a result of this study, a relative comprehensive knowledge about the nature and development of the various form of metastatic shadows has been deduced. It is rational to say that the various forms seen on the chest films represent only the various evolutionary changes of the same lesion. (Author abstract) (11 Refs)

35. ANTI-HLA ANTIBODIES DETECTED IN THE SERUM OF PATIENTS WITH GESTATIONAL TROPHOBLASTIC TUMORS (CHORIOCARCINOMAS AND INVASIVE MOLES).

Yamashita K, Ishikawa M, Shimizu T, Kuroda M
Dept. Obstetrics and Gynecology, Asahikawa Medical Coll., Asahikawa, 078-11, Japan
Gynecol Oncol; 12(3):296-301 1981

Four patients with choriocarcinomas and 19 patients with invasive moles were analyzed serially for anti-HLA antibodies. One serum out of four with choriocarcinomas and 6 sera out of 19 with invasive moles demonstrated monospecific anti-HLA antibodies and persisted as long as each patient was treated by chemotherapy. One serum which was not determined to be anti-HLA antibody was checked with the serum of one patient with choriocarcinoma. The relationship between the antibodies and tumor growth or response to chemotherapy was studied clinically, but no definite relationship was established. In the present studies, antigenicity of the trophoblastic cell itself was not established. (Author abstract) (13 Refs)

36. PREGNANCY OUTCOME AFTER MOLAR GESTATION.

Berkowitz RS, Goldstein DP
Dept. Obstetrics and Gynecology, Harvard Medical Sch., Boston, MA
Contemp Obstet Gynecol; 18(6):69-70,75,77 1981

The success of pregnancy following chemotherapy for gestational trophoblastic disease is discussed. Such therapy need not interfere with reproduction, even when uterine invasion or metastasis has occurred. Six consecutive mo of normal human chorionic gonadotropin titers demonstrates complete and sustained remission, after which the patient may become pregnant. Of 912 patients treated for hydatidiform mole, 783 later became pregnant, resulting in 511 full-term live births, 76 premature deliveries, 6 ectopic pregnancies, and 4 stillbirths. First-trimester spontaneous abortions occurred in 147 and congenital anomalies in 30. Of 186 patients treated for invasive trophoblastic disease, 118 became pregnant, resulting in 77 full-term deliveries, 4 premature deliveries, 3 ectopic pregnancies, and 1 stillbirth. First-trimester spontaneous abortion ended 24 pregnancies. Congenital malformations were diagnosed in only three infants. No patient who had two or more consecutive trophoblastic tumors subsequently achieved a normal viable pregnancy. Future pregnancy may place the patient at increased risk of recurrent trophoblastic neoplasia. (14 Refs)

MULTI-SITE STUDIES AND REVIEWS

37. PELVIC EXENTERATION FOR VULVOVAGINAL CARCINOMA.

Phillips B, Buchsbaum HJ, Lifshitz S
(c/o Buchsbaum) Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. Texas-Southwestern Medical Sch., 5323 Harry Hines Blvd., Dallas, TX, 75235
Am J Obstet Gynecol; 141(8):1038-1044 1981

Between 1964 and 1978, 16 pelvic exenterations were performed for advanced and recurrent vulvovaginal carcinoma. Eight patients had Stage III carcinoma and four had recurrent vulvar carcinoma. Ten patients had involvement of the anus/sphincter, and two had involvement of the proximal half of the urethra. There were four patients with vaginal carcinoma. Two patients with recurrent vaginal carcinoma had bladder/urethral involvement; one patient each with primary vaginal carcinoma had rectovaginal and vesicovaginal septal disease. Seven patients were alive and free of disease - six for more than 5 yr and one for 4 yr and 4 mo. Three patients died, free of disease, one each of cerebrovascular accident, traumatic subdural hematoma, and pulmonary embolus. One patient died on the ninth postoperative day of aspiration pneumonitis. The absolute 5-yr survival rate is 54%. (Author abstract) (3 Refs)

38. THE AUTOMATIC STAPLE VERSUS THE CONVENTIONAL GASTROINTESTINAL ANASTOMOSIS IN GYNECOLOGICAL MALIGNANCIES.

Delgado G
Div. Gynecologic Oncology, Georgetown Univ. Hosp. Medical Center, Washington, DC, 20007
Gynecol Oncol; 12(3):302-313 1981

Seventy-four patients with gynecologic malignancies and two with benign tumors underwent different types of gastrointestinal resections to relieve bowel obstruction or to correct fistulas. All but two of these patients had gynecologic cancer with one or more modalities of therapy prior to resection. The anastomoses of 47 patients were performed with open conventional techniques which included closure of the full thickness of the bowel. In 28 patients, the automatic stapler was used 63 times. In 3 of the 28 staple anastomosis patients, the EEA (end-to-end anastomosis) was used. In this study, the use of the staple anastomosis was shown to be as effective as the conventional method because it shortened the operating time, provided less contamination of the abdominal cavity, and provided a better blood supply. (Author abstract) (15 Refs)

39. MULLERIAN CARCINOMA. THE SYNCHRONOUS APPEARANCE OF EPITHELIAL NEOPLASIA WITHIN SEVERAL SITES OF MULLERIAN ORIGIN (MEETING ABSTRACT).

Johnson RL, Davis BW, Page DL, Burnett L
Department of Pathology, Vanderbilt University Hospital, Nashville, TN, 37232
Am J Clin Pathol; 76(3):355 1981

The phenomenon of multiple malignancy requires careful clinical and pathologic evaluation in this age of multiple modality therapy. We present our experience of three cases with synchronous appearance of multiple primary carcinoma of Mullerian derived epithelium: two cases presenting with synchronous carcinomas of at least three different anatomic sites including ovary, fallopian tube, endometrium, and cervix and a third case with apparent metachronous development of a third carcinoma of Mullerian epithelium following surgical and multiple agent chemotherapy. Mullerian carcinoma is a syndrome of multiple (3) primary carcinomas arising in Mullerian derived epithelium. Recognition of this phenomenon is necessary for adequate clinical evaluation and staging, pathologic analysis, and proper treatment regimens. In addition, the possibility of metachronous malignancy in patients with multiple carcinomas treated with combined chemotherapy and less than total surgical removal of the Mullerian system should occasion a careful follow-up. (no Refs)

40. RESEARCH ON CANCER CHEMOTHERAPY FOR HUMAN OVARIAN CLEAR CELL CARCINOMA TRANSPLANTED IN MICE - INTRATUMORAL KINETICS OF 5-FLUOROURACIL.

Koike K, Ohkawa K, Amasaki H, Terashima Y
Dept. Obstetrics and Gynecology, Jikei Univ. Sch. Medicine, Tokyo, Japan
Nippon Gan Chiryo Gakkai Shi; 16(4):627-632 1981

5-fluorouracil (5-FU) was administered (100 mg/kg x 1x, ip) to nude mice (JOA-1) bearing transplanted human ovarian clear cell carcinoma (generation 5-8), and the effects of the 5-FU were examined with respect to changes in tumor cell morphology and growth, drug distribution, and retro-transplanted tumor growth ratio. Peak intratumoral concentrations of 5-FU, 29 ug/g, were reached 15 min after a single-shot administration in mice, 4 wk after tumor transplantation, and no 5-FU was detected with the aid of bioassay method, 120 min after the injection. Compared to pretreatment, tumor cells were observed with electron microscopy to have abundant heterochromatin in nuclei, decreased numbers of free ribosomes, decreased size of mitochondria, and increased numbers of lysozyme-like dense bodies 5 min after treatment with 5-FU. No significant changes in 3H-thymidine labeling indices were observed following in vitro administration of 5-FU to the tumor cells, but significant decreases in mitotic indices were observed 48 hr after administration of the 5-FU. Retransplantation of tumors were possible in the nude mice bearing the ovarian clear cell carcinoma and treated with the 5-FU, but the growth of the retransplanted tumors was delayed about 2 wk. The results suggested that this model may be applied to clinical evaluations of pharmacological agents. (12 Refs) (In JPN)

41. HEXAMETHYLMELAMINE AND PENTAMETHYLMELAMINE TISSUE DISTRIBUTION IN M5076/73A OVARIAN CANCER-BEARING MICE.

Broggini M, Rossi C, Colombo T, D'Incalci M
(c/o D'Incalci), Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy
Cancer Treat Rep; 66(1):127-133 1982

The distribution of hexamethylmelamine (HMM), pentamethylmelamine (PMM), and their metabolites N2,N2,N4,N6-tetramethylmelamine (TMM) and N2,N4,N6-trimethylmelamine (TriMM) was investigated in different tissues of M5076/73A ovarian cancer-bearing mice given 100 mg/kg ip of either drug. The area-under-the-curve (AUC) values of HMM and PMM, expressed in ug/g x min after these drug treatments, were 2,432 and 1,296 in tumor, 6,290 and 8,141 in liver, 9,779 and 21,294 in spleen, 6,840 and 10,800 in kidney, 4,003 and 4,295 in heart, 1,569 and 1,327 in brain, 163,689 and 50,809 in adipose tissue, 88,725 and 45,070 in lymph nodes, 15,033 and 18,992 in small intestine, and 393 and 351 in plasma, respectively. The elimination rate of HMM for the different organs was similar, with a half-life of 37-48 mins; PMM disappeared with more variability, the half-life being 19-46 min. While TMM concentrations were not very different from those of HMM or PMM, TriMM was much higher in all organs evaluated, particularly the brain, where AUC values were 21-24x those of the administered drug. (Author abstract) (16 Refs)

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GYNECOLOGIC TUMORS

Diagnosis, Treatment

SERIES CT17 No. 82/06 JUNE, 1982

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VULVAR TUMORS

1. VULVAR INTRAEPITHELIAL NEOPLASIA: CORRELATION OF NUCLEAR DNA CONTENT AND THE PRESENCE OF A HUMAN PAPILLOMA VIRUS (HPV) STRUCTURAL ANTIGEN.

Crum CP, Braun LA, Shah KV, Fu YS, Levine RU, Fenoglio CM, Richart RM, Townsend DE
Div. Ob/Gyn Pathology, Columbia Univ. Coll. of Physicians and Surgeons, 630 West 168th St., New York, NY, 10032
Cancer; 49(3):468-471 1982

Immunoperoxidase localization of a human papilloma virus structural antigen (HPV) was attempted in 68 intraepithelial lesions of the vulva, 39 of which were analyzed for nuclear DNA content by microspectrophotometry. Overall, 5.9% (4/68) stained positive for HPV. Ninety per cent (35/39) of the cases tested were aneuploid, and, of these, 2.8% (1/35) stained positive for HPV. In contrast, 50% (2/4) of the polyploid lesions were positive. Hence DNA microspectrophotometry and immunoperoxidase localization of HPV are useful coparameters for distinguishing wart virus infection (condylomata) from vulvar intraepithelial neoplasia. HPV is detected infrequently within aneuploid lesions, in keeping with the concept

HE 20.3173/2:

that epithelial maturation is required for virion assembly. Whether the HPV genome exists in a nonreplicative state within the aneuploid cell population is unknown. (Author abstract) (18 Refs)

CERVICAL AND UTERINE TUMORS

2. COMPUTED TOMOGRAPHIC EVALUATION OF CARCINOMA OF THE CERVIX.

Whitley NO, Brenner DE, Francis A, Villa Santa U, Aisner J, Wiernik PH, Whitley J
Dept. Diagnostic Radiology, Univ. Maryland Hosp., 22 South Greene St., Baltimore, MD, 21201
Radiology; 142(2):439-446 1982

To assess the accuracy of computed tomography (CT) in staging advanced carcinoma of the cervix, 18 staging evaluations were performed in 16 patients with locally advanced (FIGO Stage IB-IVA) cervical carcinoma. CT staging results were compared with the results of clinical staging and postoperative staging. CT was accurate in 12/18 (66%) cases, clinical staging was accurate in 10/18 (55%) cases, and clinical staging with cystoscopy was accurate in 14/18 (78%) cases. CT staging failed to detect microscopic pelvic side-wall involvement and bladder involvement when there was no contrast material in the bladder. In the detection of para-aortic lymph node involvement by tumor, there were 12 true-negative, 4 true-positive, 1 false-positive, and 1 false-negative study (sensitivity = 80%, specificity = 92%). It is concluded that CT is equal in accuracy to other clinical staging techniques and offers the advantage of visualizing the tumor, which allows for more accurate determination of radiation portals. (Author abstract) (17 Refs)

3. A COMPARISON OF ENDOMETRIAL SAMPLING WITH THE ACCURETTE AND VABRA ASPIRATOR AND UTERINE CURETTAGE.

Goldberg GL, Tsalacopoulos G, Davey DA
Dept. Obstetrics and Gynecology, Univ. Cape Town, Cape Town, South Africa
S Afr Med J; 61(4):114-116 1982

Endometrial samples were obtained with the Accurette and the Vabra aspirator and were compared with samples obtained by dilation and curettage in 40 patients with postmenopausal bleeding. The degree of discomfort and patient acceptability of the two outpatient procedures, the adequacy of the samples for cytological and histological examination, and the cytological and histological diagnosis were compared. The Accurette and the Vabra aspirator could not be inserted in 5 out of 40 patients because of cervical stenosis. From approx 30 of the remaining 35 patients, adequate samples were obtained. Six cases of endometrial hyperplasia and three of endometrial carcinoma were diagnosed by all the methods employed, except for one case of endometrial hyperplasia in which the sample obtained with the Accurette was inadequate for h istological examination but was nevertheless adequate for cytological examination. Of the five patients in whom endometrial sampling by both the Accurette and the Vabra aspirator could not be performed because of cervical stenosis, two cases of endometrial carcinoma were found on uterine curettage. In patients with cervical stenosis, however, dilatation and curettage under general anesthesia is mandatory. The Accurette has the advantage of being less expensive and more suitable for routine endometrial sampling for the detection of endometrial hyperplasia or carcinoma and dating of the endometrium in cases of infertility. Both the Accurette procedure and Vabra aspiration appeared to be reliable methods of obtaining endometrial samples. (Author abstract) (8 Refs)

4. DIAGNOSTIC ACCURACY OF THE ACCURETTE ENDOMETRIAL SAMPLER.

Sonnendecker EW, Simon GB, Sevitz H, Hofmeyr GJ
Dept. Obstetrics and Gynecology, Johannesburg Hosp., Johannesburg, South Africa
S Afr Med J; 61(4):109-113 1982

The value of the Accurette endometrial sampler in the cytological and histological assessment of the endometrium was studied in 42 anesthetized patients. Satisfactory samples for cytological diagnosis of endometrial state were obtained in 23 patients out of 24 (96%), whereas endometrial specimens suitable for histological diagnosis were obtained in 23 out of 29 patients (79%). Immediately following Accurette sampling, conventional dilatation and curettage was performed. Histological diagnosis of Accurette samples correlated with that of formal curettage in all instances except in the detection of polyps. Cytological findings with the Accurette did not correlate with those of formal curettage in two cases. Nevertheless, interpretation of endometrial cytology, which requires specialized knowledge and experience, is shown to provide helpful information especially in cases where curettage fails to yield tissue. (Author abstract) (15 Refs)

5. DESCRIPTION OF A NEW DISPOSABLE UTERINE SAMPLER (THE ACCURETTE) FOR ENDOMETRIAL CYTOLOGY AND HISTOLOGY.

Kriseman MM
Park Lane Clinic, Parktown, Johannesburg, South Africa
S Afr Med J; 61(4):107-108 1982

A disposable, collapsible curette made from a special plastic material, devised by the author for obtaining cytological and histological samples of the uterine endometrium, is described. A simple syringe for vacuum aspiration is incorporated with the instrument. Its manifold advantages include simplicity of design and ease of application, making little demand on the operator. No additional apparatus is required for its use in outpatient clinics or as an office procedure. (Author abstract) (3 Refs)

6. THE LYMPHOCYTE-EPITHELIAL CELL RATIO IN TUBAL MUCOSA OF PATIENTS WITH CERVICAL CARCINOMA.

Geppert M, Bohle A
Pathologisches Institut, Kreiskrankenhaus, Postfach 240, 7410 Reutlingen 1, W. G ermany
Pathol Res Pract; 173(1/2):82-87 1981

The lymphocytes in the luminal subepithelial basement membrane of the uterine tube from patients with cervical carcinoma were counted, and the results compared with those obtained from women of the same age but without cervical carcinoma to determine whether a relationship exists between the emigration of lymphocytes into the tubal epithelium and the clinical diagnosis of cervical carcinoma. The comparison indicated that the number of lymphocytes migrating into the tubal epithelium during the secretory and the proliferative phase in women with cervical carcinoma is significantly lower than that in healthy women from the control group. The differences during the secretory phase were particularly pronounced. The lymphocyte

count in patients with cervical carcinoma was only one third that of the healthy women in the control group. Assuming that an immunologic defect is determinative for the development of carcinoma, a decline in the number of lymphocytes migrating into the tubal epithelium can be interpreted as the reflection of an immunologic deficiency. It is possible that a disturbance in the lymphocyte: epithelial cell ratio in this stage of life could indicate a disposition for those tumors the incidence of which is high in this age group (eg, squamous cell carcinoma of the cervix). Further study is necessary to establish whether these cells be classified as B or T lymphocytes. (Author abstract) (16 Refs)

7. LASER CONIZATION VERSUS COLD KNIFE CONIZATION.

Larsson G, Ahn P, Grundsell H
Dept. Obstetrics and Gynecology, Univ. Hosp., Lund, Sweden
Surg Gynecol Obstet; 154(1):59-61 1981

This prospective, randomized study compares, for the first time, measured blood loss at conization and within 24 hr after using either the cold knife technique or the carbon dioxide laser scalpel. One hundred and ten consecutive patients were evaluated. The median blood loss in the laser group of 55 patients was 4.6 ml at, and within 24 hr after operation compared with 30.1 ml in the cold knife group of 55 patients. More important, however, is that the corresponding figures for the range of bleeding were 0.4 to 155.4 ml and 5.6 to 1,570.9 ml, respectively. The incidence rate for bleeding complications requiring surgical intervention was 1.8% for the laser group and 14.6% for the cold knife group. This difference was statistically significant, p less than 0.015-Fischer's exact test. Conization for treatment of premalignant changes of the cervix uteri will probably remain the treatment of choice for some time to come. It is our opinion that, in the future, laser conization will replace cold knife conization. (Author abstract) (7 Refs)

8. URINARY BLADDER COMPLICATIONS FOLLOWING WERTHEIM OPERATIONS - RECOMMENDATIONS FOR A CONTROLLED FOLLOW-UP WITH COMPARABLE CONDITIONS.

Christ F, Wagner U, Behr J
Universitats-Frauenklinik Charlottenburg, Pulsstr. 4-14, 1000 Berlin 19, W. Germany
Geburtshilfe Frauenheilkd; 41(11):754-758 1981

At defined times prior and following a Wertheim operation for cancer of the uterine cervix the patients were investigated for the functional parameters of the lower urinary tract. The residual urine was determined. Stress incontinence and urgency incontinence were measured with urethrocystometry. The sensitivity and the micturition were evaluated from subjective data. The results of 237 investigations in 192 operated women are described and compared to previous papers on the subject. Stress incontinence increased to double the pre-operative incidence following the Wertheim operation. An urgency incontinence was quite rare. A lack of feeling of fullness to the bladder as a sign of disturbed bladder sensitivity was present 5 mo post-operatively in 6 of 45 patients (13%). This was present in only 1 of 119 patients (1%) after 5 yr, 1/3 of the women had difficulty with spontaneous micturition 5 mo following the operation. One-tenth of the women had difficulty with spontaneous micturition 5 yr after the operation. There was no residual urine 5 mo after the operation in 9/10 of the patients and 5 yr following the operation almost 100% of the patients had no residual urine. It was noted that difficulty with spontaneous micturition with residual urine and urgency incontinence did not necessarily result in concomitant bacteriuria. Suggestions are presented how future investigations with similar questions may lead to comparable results. (Author abstract) (31 Refs) (In GER)

9. THE VALUE OF ADJUVANT CHEMOTHERAPY IN ADVANCED CERVICAL CANCER: FIRST RESULTS OF A PROSPECTIVE RANDOMIZED STUDY.

Richter P
Frauenklinik, Medizinische Akademie 'Carl Gustav Carus' Dresden, Fetscherstrasse 74, DDR-8019 Dresden, E. Germany
Arch Geschwulstforsch; 52(2):117-122 1982

First results of a randomized study of the value of adjuvant chemotherapy in treatment of cervical carcinoma (CC) are reported. Forty-nine women with histologically confirmed advanced CC with metastatic involvement of the iliac and/or paraaortic lymph nodes were studied. All patients underwent radical hysterectomy with lymphadenectomy, followed by radiotherapy (RT: tumor dose 6,000 rads). Patients with metastatic paraaortic nodes received lumbar irradiation (5,000 rads). Group A (23 patients, av age 39.5 yr) received chemotherapy. Group B (26 patients, av age 46 yr) received only surgical and RT. Chemotherapy consisted of cyclophosphamide (15 mg/kg), methotrexate (0.3 mg/kg), and vincristine (0.01 mg/kg). All three drugs were administered in five short-term infusions during the first 6 wk. Subsequently treatments were administered as massive-dose injections at 4-wk intervals up to 30 wk. After an av observation period of 33 mo in Group A and 27.6 mo in Group B 65% of patients were tumor-free. Death due to tumor recurrence occurred in 25-26% of patients in both groups. Av survival time among patients who died of tumor was 16 mo in Group A an 19 mo in Group B. No evidence of tumor was found in any of the other patients who died. Results show no advantage to the adjuvant therapy used; no general conclusion regarding chemotherapy could be reached. (27 Refs) (In GER)

10. IMPROVEMENT IN CERVICAL DYSPLASIA ASSOCIATED WITH FOLIC ACID THERAPY IN USERS OF ORAL CONTRACEPTIVES.

Butterworth CE, Hatch KD, Gore H, Mueller H, Krumdieck CL
Dept. Nutrition Sciences, Univ. Alabama, Birmingham, AL
Am J Clin Nutr; 35(1):73-82 1982

Forty-seven young women with mild or moderate dysplasia of the uterine cervix (cervical intraepithelial neoplasia) diagnosed by cervical smears, received oral supplements of folic acid, 10 mg, or a placebo (ascorbic acid, 10 mg) daily for 3 mo under double-blind conditions. All had used a combination-type oral contraceptive agent for at least 6 mo and continued it while returning monthly for follow-up examinations. All smears and a biopsy obtained at the end of the trial period were classified by a single observer without knowledge of treatment status using an arbitrary scoring system (1 normal, 2 mild, 3 moderate, 4 severe, 5 carcinoma in situ). Mean biopsy scores from folate supplemented subjects were significantly better than in folate-unsupplemented subjects (2.28 versus 2.92, respectively; p less than 0.05). Final versus initial cytology scores were also significantly better in supplemented subjects (1.95 versus 2.32, respectively; p less than 0.05), unchanged in patients receiving the placebo (2.27 versus 2.30, respectively). Before treatment the mean red cell folate concentration was lower among oral contraceptive agent users than nonusers (189 versus 269 ng/ml, respectively; p less than 0.01) and even lower among users with dysplasia (161 versus 269 ng/ml, re-

spectively; p less than 0.001). Morphological features of megaloblastosis were associated with dysplasia and also improved in folate supplemented subjects. These studies indicate that either a reversible, localized derangement in folate metabolism may sometimes be misdiagnosed as cervical dysplasia, or else such a derangement is an integral component of the dysplastic process that may be arrested or in some cases reversed by oral folic acid supplementation. (Author abstract) (24 Refs)

11. ESTROGEN AND PROGESTERONE RECEPTORS AND RESPONSE TO AN ANTIESTROGEN OF POST-MENOPAUSAL ENDOMETRIAL CARCINOMA AND METASTATIC BREAST CANCER.

Baulieu EE, Mortel R, Levy C, Namer M, Robel P
Lab. Hormones, 94270 Bicetre, France
Excerpta Med Int Congr Ser; 551:234-245 1981

The effects of tamoxifen (TAM) on estradiol (ER) and progesterone receptor (PR) sites were measured in endometrial cancers and in skin metastases of breast cancers. In a group of 43 postmenopausal women with endometrial carcinoma, two biopsies from each were studied: at time of referral and during surgery or just prior to radiotherapy. Fifteen patients received TAM 40 mg/day po for 5-7 days after the first biopsy and the second biopsy was performed 12-18 hr after the last dose. Ten patients ingested 10 mg TAM 8 and 4 hr prior to the second biopsy. Total ER concentration (cytosol + nuclear) in tumors was similar to that in late proliferative phase of normal endometrium. Values for PR concentration were low and comparable to those found in the secretory phase of the normal menstrual cycle. No hormonal correlations of receptors was found. Where TAM immediately preceded biopsy, the ratio of cytoplasmic to nuclear receptor shifted in favor of nuclear receptors. In patients treated with TAM 12-18 hr before biopsy, PR sites increased in all but four samples, while in patients treated immediately before biopsy, no increase in PR was observed. TAM did not influence levels of ornithine decarboxylase or estradiol dehydrogenase. In a somewhat similar study in 21 women with advanced metastatic breast cancer, ER and PR were absent or low in 9; in 10/12 of the ER positive cases, only 2 were PR negative. There was a significant positive correlation between ER and PR in untreated tumors. After TAM administration, available ER sites were greatly decreased. No PR receptor change was observed where ER was less than 20 femtomole/mg cytosol protein. Among the remaining cases, 7/12 showed an increase of PR of greater than 100 femtomole/mg cytosol protein. (35 Refs)

12. ENDOMETRIAL ADENOCARCINOMA METASTATIC TO THE SCALP: REPORT OF TWO CASES.

Debois JM
Dept. Radiation Oncology, St Norbertus Hosp., B-2570 Duffel, Belgium
Arch Dermatol; 118(1):42-43 1982

Two patients had late metastatic endometrial carcinoma and skin metastases of the scalp. Endometrial carcinoma metastatic to the skin is rare, although involvement of the scalp in tumor metastases in general has been emphasized previously. (Author abstract) (15 Refs)

13. PROTECTION AGAINST ENDOMETRIAL CARCINOMA BY COMBINATION-PRODUCT ORAL CONTRACEPTIVES.

Hulka BS, Chambless LE, Kaufman DG, Fowler WC, Greenberg BG
Dept. Epidemiology, Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27514
JAMA; 247(4):475-477 1982

Seventy-nine patients with endometrial carcinoma were compared with 203 control subjects regarding their use of combination-product oral contraceptives (OCs). Overall, 6.3% of patients and 15.3% of control subjects had used these products. The risk of endometrial cancer for users of OCs was less than half the risk of nonusers. Five yr or more of use reduced the risk to a third. Recent users were strongly protected, whereas discontinuation resulted in risks returning to those of nonusers. Furthermore, OCs with predominantly progestational effects or intermediate formulations produced greater protection than those with predominantly estrogens. This pattern of results is biologically consistent with a protective effect of combination-product OCs against endometrial carcinoma. (Author abstract) (13 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

14. RADIOIMMUNOASSAY OF THE NORMAL SERUM GLYCOPROTEIN (CX 1) IN MONITORING OVARIAN MALIGNANCY.

Wass M, Searle F, Bagshawe KD
Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England
Eur J Cancer Clin Oncol; 17(12):1267-1273 1981

A glycoprotein designated CX 1, of mol wt 80,000, has been extracted from adenocarcinomas of the ovary and its measurement by radioimmunoassay established. CX 1 is present in the normal ovary and in normal serum. It is present in various non-ovarian carcinomas but in much greater amount in ovarian adenocarcinoma and in ascitic fluid associated with this cancer. Increased concentrations are found in the serum of patients with various cancers. In about 60% of patients with Stage III and IV ovarian adenocarcinoma, serum values are elevated and they correlate with the course of the disease, providing information which probably has clinical value. (Author abstract) (13 Refs)

15. TUMOR MARKERS IN INCLUSION CYSTS OF THE OVARY.

Blaustein A, Kaganowicz A, Wells J
Dept. Pathology, Booth Memorial Medical Center, 56-45 Main St., Flushing, NY, 11355
Cancer; 49(4):722-726 1982

The immunoperoxidase method was used to determine whether carcinoembryonic antigen, beta subunit of HCG placental lactogen, pregnancy-associated alpha-2 glycoprotein, and pregnancy-specific beta-1 glycoprotein could be found in inclusion cysts of the ovary. These tumor markers are found in the serum of patients with common epithelial carcinomas of the ovary and inclusion cysts are considered to be the origin of these tumors. Placental lactogen was found in 56 of 118 inclusion cysts, beta subunit of HCG in 4 of 141 cysts, alpha-2 glycoprotein in 5 of 141, and beta-1 glycoprotein in 2 of 118. It was concluded that primitive cells in inclusion cysts elaborate

the same tumor markers found in serous cystadenoma and cystadenocarcinoma of the ovary. This observation, although not proving origin of tumor from the inclusion cyst, demonstrates a significant characteristic shared in common by all three. (Author abstract) (15 Refs)

16. USE OF HIGH DOSE CIS-DICHLORODIAMMINE PLATINUM (II) (NSC-119875) FOLLOWING FAILURE ON PREVIOUS CHEMOTHERAPY FOR ADVANCED CARCINOMA OF THE OVARY.

Barker GH, Wiltshaw E
Central Middlesex Hosp., London NW10, England
Br J Obstet Gynaecol; 88(12):1192-1199 1981

The compound cis-dichlorodiammine platinum II (cisplatin) in high dose was given to 40 patients with advanced carcinoma of the ovary, 31 had been previously treated with alkylating agents or various chemotherapy regimens excluding cisplatin and 9 patients had tumors resistant to low dose cisplatin regimens. The high dose regimen consisted of cisplatin given at 100 mg/m2 with 24 hr pre- and post-treatment hydration, at monthly intervals up to a max of five doses. Seventeen of the 31 patients (55%) showed a therapeutic response including 25% who had complete regression of tumor. The median duration of complete remissions was 10 mo. Unfortunately, patients who had already been exposed to cisplatin at low doses (20 mg/m2) responded less well, only two out of nine (22%). Even at this late stage of disease, seven patients showed a good enough response to undergo further surgery and of these three were macroscopically clear of tumor and in two patients multiple biopsy material failed to show residual tumor microscopically. (Author abstract) (18 Refs)

17. MEDICAL RESEARCH COUNCIL STUDY ON CHEMOTHERAPY IN ADVANCED OVARIAN CANCER.

Medical Research Council's Working Party on Ovarian Cancer (c/o the Editor), British Journal Obstetrics and Gynecology, 27 Sussex Place, Regent's Park, London, NW1 4RG, England
Br J Obstet Gynaecol; 88(12):1174-1185 1981

A total of 264 eligible patients with advanced ovarian cancer were randomized to single or triple agent cytotoxic therapy; 261 were available for analysis. The treatments were continuous oral cyclophosphamide (arm S), and a combination of oral cyclophosphamide, hexamethylmelamine and methotrexate on a pulsed basis (arm T). Mortality attributed to cancer was slightly lower on arm T ($p = 0.06$), but this was offset by the greater toxicity of this regimen, and overall survival and activity index were similar on the two arms. There was thus little evidence of greater clinical benefit on the triple agent regimen. Tumor mass removed at operation, extent of remaining tumor and age all showed significant correlation with prognosis. Survival was longer in patients whose disease responded to either therapeutic regimen. (Author abstract) (12 Refs)

18. INFLUENCE OF ASCITES ON THE PHARMACOKINETICS OF HEXAMETHYLMELAMINE AND N-DEMETHYLATED METABOLITES IN OVARIAN CANCER PATIENTS.

D'Incalci M, Beggiolin G, Sessa C, Mangioni C
Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62-20157 Milan, Italy
Eur J Cancer Clin Oncol; 17(12):1331-1335 1981

Levels of hexamethylmelamine (HMM) and its metabolites pentamethylmelamine (PMM), N2N2N4N6 tetramethylmelamine (TMM) and N2N4N6 trimethylmelamine (TriMM) were determined in plasma of 31 patients with advanced ovarian cancer receiving HMM. In 14 of them with ascites the drug metab olites PMM, TMM and TriMM were assayed in this fluid. Both in plasma and in ascites a GLC method with nitrogen detection was applied after extraction with n-hexane and ethyl acetate at pH 11.5. Plasmatic HMM T/2alpha and T2/beta were respectively 47 +-6 and 403 +-37 min. Mean AUC 0 to 12 hr values +- SEM, expressed in ug/ml x min, were 312 +-95 for HMM, 117 +-32 for PMM, 260 +-50 for TMM and 311 +-82 for TriMM. AUCs of HMM, PMM, TMM and TriMM in ascites calculated up to 6 hr were 78 +-13, 31 +-7, 60 +-12 and 129 +-38 ug/ml x min respectively. The presence of ascites, the patient's age, the concomitant administration of adriamycin and cyclophosphamide and fatness did not appear to influence the kinetic behavior of HMM and metabolites. HMM was not detectable in urine and PMM, TMM and TriMM accounted for less than 1% of the HMM dose. (Author abstract) (10 Refs)

19. HEXAMETHYLMELAMINE DISTRIBUTION IN PATIENTS WITH OVARIAN AND OTHER PELVIC CANCERS.

D'Incalci M, Farina P, Sessa C, Mangioni C, Garattini S
Instituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy
Cancer Treat Rep; 66(2):231-235 1982

The distribution of hexamethylmelamine (HMM) was investigated in surgical biopsies from 12 patients with pelvic cancer who were given an oral dose of 200 mg at 2-24 hr before the operation. The highest concentrations of HMM were found in tissues, such as omentum and sc tissue, that have a predominant lipidic component. HMM concentrations in the primary tumor were lower than in other tissues and were similar to those in plasma. HMM concentrations in metastases appeared to be higher than in the primary tumor, and in metastases with a diameter less than 3 mm, drug levels were 2 to 10 times those in larger ones. Plotting the HMM concentrations vs time, utilizing the data from different patients, the elimination half-lives were found to be 9.05, 8.82, and 8.53 in plasma, tumor, and sc tissue, respectively. (Author abstract) (19 Refs)

20. HIGH-DOSE MEDROXYPROGESTERONE ACETATE (MPA) IN ADVANCED CHEMOTHERAPY-RESISTANT OVARIAN CARCINOMA: A PHASE II STUDY.

Aabo K, Pedersen AG, Hald T, Dombernowsky P
Dept. Chemotherapy R II, Finsen Inst., 49-Strandboulevarden, DK-2100 Copenhagen, Denmark
Cancer Treat Rep; 66(2):407-408 1982

The Phase II trial of high-dose medroxyprogesterone acetate (MPA: 500 mg/square meter/day in 3 fractions, po) was carried out in 30 patients (39-72 yr old) with histologically verified Stage III-IV ovarian adenocarcinoma. The duration of MPA treatment was 1-6 mo. Of 27 evaluable patients, only 1 had greater than 50% reduction of metastatic neck lymph nodes and of epigastric mass. There was no MPA-induced toxicity. (5 Refs)

21. OVARIAN TUMORS IN CHILDREN AND ADOLESCENTS.

Liu B
Dept. Obstetrics and Gynecology, Friendship Hosp., Beijing, People's Republic of China
Zhonghua Fuchanke Zazhi; 16(2):104-107 1981

Clinicopathological findings and treatment are described for 82 cases (patients, 8-19 yr old) treated between 1959 and 1978. The majority of tumors were germ cell tumors (57.3%), common epithelial tumors (20.7%) and tumor-like conditions such as cysts (15.9%). the most common symptom was abdominal pain (91.5%). Tumor was palpable by patient in 41.5% (34/82) of cases, and tumor size ranged from 6 cm in diameter to a size comparable to full-term pregnancy, with 85.4% (70/82) of cases over 10 cm in diameter. Tumors were unilateral or bilateral. Treatment was by surgical removal. Among this series, there were 14 malignant cases (17.1%), 6 of whom died from tumor recurrence following treatment, with a mortality rate of 42.9%. Incidence rate, clinical symptoms, malignancy rate, relationship of pathology to prognosis, diagnosis and treatment of childhood and adolescent ovarian tumors are discussed. (16 Refs) (In CHI)

TROPHOBLASTIC DISEASE

22. CLINICAL PATHOLOGICAL AND ROENTGENOLOGICAL MANIFESTATIONS OF PULMONARY METASTASIS OF CHORIOCARCINOMA AND MALIGNANT MOLE.

Song H, Wu B, Hu M, Su X
Dept. Obstetrics Gynecology, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Zhonghua Fuchanke Zazhi; 16(2):65-68 1981

Early metastasis, especially lung metastasis, is a characteristic feature of choriocarcinoma and malignant mole. Consequently, clinicopathological and radiological evaluations are important in the diagnosis, clinical staging and prognosis of lung metastasis of choriocarcinoma and its malignant mole. Radiological and clinicopathological findings are described for 429 cases of choriocarcinoma and 441 cases of malignant mole treated between 1949 and 1975. A total of 3,915 chest x-ray films (av 4.5 per case) were taken and studied. Diagnosis was confirmed by pathological and clinical examination. Pulmonary arteriography was also performed in all excised lung specimens (including some autopsy cases) in order to understand the pathogenesis of the pulmonary artery during lung metastasis. Results showed that roentgenological manifestations were different for choriocarcinoma and malignant mole. District lung metastasis was observed in 82.5% (354/429) of the malignant mole group. Due to the low mortality in malignant mole, pathological and autopsy comparisons were made primarily in the choriocarcinoma series. (7 Refs) (In CHI)

23. GESTATIONAL TROPHOBLASTIC DISEASE: MORPHOLOGY AND PATHOGENESIS.

Brewer JI, Mazur MT
Dept. Obstetrics and Gynecology, Northwestern Univ. Medical Sch., Chicago, IL
Excerpta Med Int Congr Ser; 551:398-404 1981

Morphological aspects in the development of choriocarcinoma and hydatidiform mole are discussed. Pregnancies in six patients with choriocarcinoma progressed normally until the onset of symp toms at 17, 24, 26, 32, 35, and 1 wk after term delivery at 40 wk. Initial symptoms were produced by metastatic lesions vagina (3), brain (2), lungs (1). Microscopically in 5/5 placentas that appeared normal grossly, small primary choriocarcinoma lesions were found by extensive examination. Observations of these patients revealed that choriocarcinoma can arise from the chorionic villi at any time during a seemingly normal pregnancy, that it can be present for some time without producing symptoms referable to the uterus or the pregnancy, and that in its earlier stages of development it is associated with villi. Cytogenetic studies of hydatidiform mole have revealed chromosomal anomalies in some and normal karyotypes in others. Partial mole by morphologic criteria does not give rise to invasive mole and choriocarcinoma. Observations reported indicate that, from a morphologic standpoint, hydatidiform mole is a single entity. (6 Refs)

24. PLACENTAL PROTEINS (SP1, HCG, PP5), AND ALPHA2-PAG IN TROPHOBLASTIC DISEASES.

Than GN, Bohn H, Csaba IF, Szabo DG, Karg NJ, Gocze P
(c/o Csaba) Dept. Obstetrics and Gynecology, Univ. Medical Sch., Edesanyak utja 17, P.O. Box 89, H-7624 Pecs, Hungary
Arch Gynecol; 231(1):33-39 1981

Monitoring system for patients with trophoblastic tumor is discussed. Pregnancy-specific beta-1glycoproterin (SP1), pregnancy-associated alpha-2 glycoprotein (alpha2-PAG), beta subunit of human chorionic gonadotropin (hCG), and the placental protein 5 (PP5) soluble protein specific for placental tissue are regularly monitored in patients. A total of 455 serial serum samples from 41 patients with trophoblastic tumor (26 hydatidiform mole, 8 chorioadenoma, 7 choriocarcinoma) were analyzed. SP1, hCG, and PP5 were measured by the specific radioimmunoassay. Alpha2-PAG was measured by electroimmunoassay. Sp1 levels were high in 36 patients, hCG levels in 35 patients, and alpha2-PAG levels in 29 patients. PP5 was found only in patients with a hydatidiform mole and disappeared from sera within a few hr after evacuation. SP1 and hCG levels decreased during treatment but seronegativity was reached only after some mo. hCG disappeared from serum more slowly. In some patients only one of the tumor markers was present during follow-up. Careful monitoring including measurements of serum SP1 and hCG levels is important. Positive correlation between alpha2-PAG, hCG, SP1 and clinical course was found in only 80% of patients. Case reports of a 42-yr-old patient with uterine choriocarcinoma treated by hysterectomy and chemotherapy, and of a 41-yr-old patient treated for choriocarcinoma which developed shortly after a hydatidiform mole, are presented. (21 Refs)

25. BIOLOGICAL AND BIOCHEMICAL PROPERTIES OF HUMAN CHORIONIC GONADOTROPIN FROM URINE OF PATIENTS WITH HYDATIDIFORM MOLE AND ITS RADIOIMMUNOASSAY.

Nishimura R, Hamamoto T, Tanabe K, Takemori M, Ashitaka Y, Tojo S
Dept. Obstetrics and Gynecology, Kobe Univ. Sch. Medicine, Kobe, Japan
Nippon Naibunpi Gakkai Zasshi; 57(11):1632-1644 1981

Human chorionic gonadotropin (hCG) was extracted from the urine of four women (21, 24, 24, and 26 yr old, respectively) prior to removal of hydatidiform moles. The hCG was extracted and purified from the urine samples, and various biological and biochemical tests were performed with the hydatidiform hCG. The tests included diethylaminoethanol-cellulose

ion-exchange chromatography, sephadex G-100 gel-chromatography, sodium dodecyl sulfate disc electrophoresis, amino acid analysis, immunological activity of the hCG, biological activity of the hCG with respect to young rat ovaries, receptor assays, and in vivo Parlow rat ovaries, and radioimmunoassay (RIA; antiserum or 125I labeling). Immunological and biological activities of the urinary hCG from the four patients was equivalent to those observed for urinary hCG from normal pregnant women. Amino acid analysis indicated that the hydatidiform mole hCG and normal pregnancy hCG were very similar and the hydatidiform mole hCG was constructed of alpha and beta subunits. An RIA system for hydatidiform mole urinary hCG was established, and this method correlated well with the usual methods used to determine concentrations of serum hCG in normal pregnant women and in patients with trophoblastic diseases. (19 Refs) (In JPN)

26. IMMUNOLOGY AND TREATMENT OF TROPHOBLASTIC NEOPLASIA.

Bagshawe KD

Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England

Excerpta Med Int Congr Ser; 551:392-397 1981

Blood group analysis and management of trophoblastic neoplasia are discussed. A blood group incompatible mating has twice the risk of resulting in choriocarcinoma as a compatible mating. Where choriocarcinoma occurs after a non-mole pregnancy the percentage mortality is fourfold greater for incompatible as for compatible matings. Group AB women who develop choriocarcinoma after any pregnancy have a less favorable prognosis than patients of other blood groups. Patients whose consort is group AB, or to a lesser extent group B, have a better than av prognosis. A marked mononuclear cell reaction is prognostically favorable, but often difficult to assay. Patients with advanced disease before treatment may be immunosuppressed and be disadvantaged because of this. Of 28 patients with choriocarcinoma treated with skin grafts from their husbands, all showed delayed rejection times. Time elapsed between end of antecedent pregnancy and start of chemotherapy is of considerable prognostic importance. Prophylactic therapy for mole, human chorionic gonadotropin monitoring and treatment of selected patients, sequential therapy vs stratification, CNS metastases and prophylaxis, and surgery for resistant disease are also discussed. (9 Refs)

27. BENIGN MOLAR PREGNANCIES: PULMONARY COMPLICATIONS.

Huberman RP, Fon GT, Bein ME

Dept. Radiological Sciences, Univ. California Los Angeles Center for Health Sciences, Los Angeles, CA, 90024

AJR; 138(1):71-74 1982

Cardiopulmonary dysfunction has been observed after the removal of benign hydatidiform mole. Of 60 cases reviewed with benign trophoblastic disease, 5 developed respiratory complications. Two patients developed pulmonary edema that progressed to adult respiratory distress syndrome. Autopsy of two patients showed no evidence of pulmonary trophoblastic emboli. Possible etiologies for the pulmonary findings, including trophoblastic emboli, hypervolemia, disseminated intravascular coagulation, and hyperthyroidism, are discussed. (Author abstract) (14 Refs)

28. GENETICS IN GESTATIONAL TROPHOBLASTIC DISEASE.

Lawler SD

Dept. Cytogenetics and Immunogenetics, Inst. Cancer Res., London, England

Excerpta Med Int Congr Ser; 551:409-412 1981

The pathogenetics of gestational trophoblastic disease are discussed. Choriocarcinoma can follow the birth of a normal male or female child Invasive mole or choriocarcinoma can follow a pregnancy with a hydatidiform mole. Cytogenetic and biochemical marker studies show complete moles have no genetic contribution from the female parent, are diploid and, except in rare cases, have a female sex chromosome constitution and are homozygous for the genetic contribution of the male parent. In typical cases, complete mole was heterozygous for phosphoglucomutase 1, acid phosphatase, glyoxalase, esterase D, and phosphoglycolate phosphatase (PGP). Maternal exclusion was shown at the PGP locus patient type 1, husband 2-1 and male 2. All partial moles studied were triploid. In all such cases, findings were compatible with fertilization of a haploid egg by two sperms. Partial moles, in contrast to complete moles, are often heterozygous, a maternal contribution was identified, and the trisomic state was sometimes identified by enzyme pattern. Spontaneously aborted triploids, like partial moles, show a deficiency of the XYY chromosome complement; the XXY to XXX ratio favors a preponderance of origin by diandry in both triploid abortuses and partial moles. Although all cases of hydatidiform moles studied that required chemotherapy were complete moles, partial moles may also require such therapy. (15 Refs)

29. HYDATIDIFORM MOLE IN THE UNITED STATES (1970-1977): A STATISTICAL AND THEORETICAL ANALYSIS.

Hayashi K, Bracken MB, Freeman DH, Hellenbrand K

(c/o Bracken) Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, 60 College St., New Haven, CT, 06510

Am J Epidemiol; 115(1):67-77 1982

The incidence of hydatidiform mole and some epidemiologic features of the diseas e in the United States were studied. Data for the present study were obtained from the Hospital Discharge Survey (1970-1977) of the National Center for Health Statistics. The estimated incidence of hydatidiform mole over the 8-yr period was 108.4 per 100,000 pregnancies (SE = 10.3) or 1 case in every 923 pregnancies. There was an apparent increase in the incidence rate from 1970 to 1975, but the rate dropped slightly after 1975. The distribution of hydatidiform mole by maternal age showed the highest rate among women 35 yr and older, and the second highest rate among women aged 15-19. The distribution by maternal age found for the entire sample was also apparent within each race category. Overall, black women appeared to have an incidence rate half that of white women. Regional differences in the United States were observed in spite of race and age adjustment. Existing studies are reviewed in light of morphologic and cytogenetic classification schemes and a recent hypothesis for the androgenetic origin of hydatidiform mole. A fresh approach to the epidemiology of hydatidiform mole which combines epidemiologic and genetic studies is indicated. (Author abstract) (44 Refs)

MULTI-SITE STUDIES AND REVIEWS

30. CLINICAL EFFICACY OF CT AND US IN EVALUATING GYNECOLOGIC TUMORS.

Coulam CM, Julian CG, Fleischer AC
(c/o Fleischer) Dept. Radiology, Vanderbilt Univ. Sch. Medicine, Nashville, TN
Appl Radiol; 11(1):79-82,84-87 1982

Diagnostic efficacy of computed tomography (CT) and ultrasonography (US) were compared in a study of 37 patients with suspected gynecologic tumor who were examined by both techniques within 1 wk. Surgical exploration, performed within 2 wk following diagnostic studies, revealed 22 ovarian carcinomas, 5 uterine carcinomas, 3 benign ovarian cysts, 3 lymphomas, and 4 miscellaneous tumors. The two scanning methods were compared in relation to gynecological objectives concerning detection, location, size, origin, involvement, and nature of the pelvic mass. Information required to manage patients with a known or suspected gynecologic mass can be obtained by either CT or US in 49% of cases. In 19% one or the other modality may fail to detect some lesions, such as subdiaphragmatic metastases, or may not add information that was not apparent clinically. In approx one third of cases one modality (more often CT) was more helpful than the other. (7 Refs)

31. MUSCLE AND MUSCULOCUTANEOUS FLAPS IN GYNECOLOGIC SURGERY.

Nahai F
Dept. Plastic Surgery, Emory Univ. Clinic, Atlanta, GA
Clin Obstet Gynecol; 24(4):1277-1317 1981

The principles and procedures for muscle and musculocutaneous flap transposition in the pelvic region are discussed. Photographs and diagrams demonstrate manipulation of the muscular and vascular anatomy of this region. Flaps based on vascular pedicles that are located outside the usual fiel d of surgical resection or irradiation for female genital tract carcinoma offer a one-stage method of reconstruction of the area after such treatment. (14 Refs)

32. RHABDOMYOSARCOMA OF THE FEMALE UROGENITAL TRACT.

Hays DM, Raney RB, Lawrence W, Gehan EA, Soule EH, Tefft M, Maurer HM
Children's Hosp. Los Angeles, P.O. Box 54700, Terminal Annex, Los Angeles, CA, 90054
J Pediatr Surg; 16(6):828-834 1981

Results of management of 27 female patients (up to 21 yr old) with rhabdomyosarcoma of the urogenital tract are presented. Pelvic exenteration followed by irradiation and a 2-yr course of prophylactic multiple agent chemotherapy (vincristine, dactinomycin, cyclophosphamide) for primary bladder or vaginal tumors were found to be effective. Partial cystectomy for bladder rhabdomyosarcoma was inferior to exenteration, although the beneficial effects of chemotherapy-radiotherapy were apparent. Patients treated by similar limited surgical procedures for bladder rhabdomyosarcoma prior to chemotherapy had relapse rates of almost 100%. Six of eight patients with nondisseminated primary vaginal tumors did not have initial complete tumor resection; 6/8 had inadequate or no radiotherapy. The lack of mortality in this group after observations of 36-74 mo, all patients being tumor-free, indicates that vaginal tumors are particularly susceptible to chemotherapy. A variety of different surgical procedures were found to be effective against this tumor. Patients with vulval primaries were treated surgically by complete tumor excision and have done well on prophylactic chemotherapy with or without radiotherapy. In 11 patients subjected to lymphadenectomy for bladder, vaginal, or vulval lesions, only one dissection was positive. (17 Refs)

SELECTED PRE-CLINICAL STUDIES

33. EVALUATION OF IN VIVO AND IN VITRO RESPONSES OF ENDOMETRIAL ADENOCARCINOMA TO PROGESTINS.

Holinka CF, Deligdisch L, Deppe G, Fleming H, Namit C, De la Pena MM, Gurpide E
Dept. Obstetrics and Gynecology, Mount Sinai Sch. Medicine, New York, NY, 10029
Adv Exp Med Biol; 138:365-376 1982

In vivo and in vitro effects of progestins on endometrial cancer (EC), correlation between progesterone receptor levels and histologic changes after medroxyprogesterone acetate (MPA) administration, and properties of monolayer cultures of epithelial cells from endometrial adenocarcinoma (EA) were studied. Results of MPA treatment on EA and of estradiol 17beta dehydrogenase activity in EC in organ culture are presented. (34 Refs)

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VULVAR TUMORS

1. PELVIC LYMPHADENECTOMY IN INVASIVE SQUAMOUS-CELL CARCINOMA OF THE VULVA.

de Graaff J, Stolk JG, Janssens J
Afdeling Verloskunde en Gynaecologie, Academisch Ziekenhuis van de Vrije, Amsterdam, The Netherlands
Ned Tijdschr Geneeskd; 125(21):829-833 1981

Forty-four patients (av age 67.9 yr) with invasive squamous-cell carcinoma of the vulva were subjected to radical vulvectomy with bilateral inguinal lymphadenectomy and bilateral pelvic lymphadenectomy. Stage I was diagnosed in 17 patients, Stage II in 17 and III in 10. Lymph node metastases were found in 15/44 patients: in 8/33 with lateral carcinoma and in 7/11 with central carcinoma. The incidences of lymph node metastases were 1/17 in Stage I, 7/17 in Stage II and 7/10 in

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III. Inguinal lymph node meta stases were found in 14/15 patients, including those who also had iliac lymph node metastasis, and only iliac lymph node metastasis was found in 1 patient. The primary carcinoma was located in the labium in 8/15 patients, in the clitoris in 7/15. The patients with lymph node metastases were subjected to radiotherapy. Five of the 15 patients with lymph node metastases died within 0.25-6 yr (one of them died of intercurrent disease), the 10 others were alive 0.75-10 yr after treatment. Pelvic lymphadenectomy is recommended in patients with carcinoma of the clitoris, with carcinoma having spread to the inside of the labium minus, and with large carcinoma of the labia (Stages II and II), and in patients with tumor cells in the inguinal lymph nodes. (16 Refs) (In DUT)

2. ALVEOLAR SOFT PART SARCOMA OF THE VULVA: REPORT OF FIRST CASE AND REVIEW OF LITERATURE.

Shen JT, D'ablaing G, Morrow CP

Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, St. Luke's-Roosevelt Hosp. Center (Columbia Univ.), New York, NY, 10019

Gynecol Oncol; 13(1):120-128 1982

A case of primary alveolar soft part sarcoma of the vulva is reported, with review of literature on this tumor arising from other parts of the human body. The patient is a 62-yr-old caucasian secundigravida, with a 4-cm asymptomatic tumor in the right labium minus. Histology shows polygonal cancer cells with granular cytoplasm, forming alveolar patterns. Radical vulvectomy with complete dissection of the right groin and superficial dissection of the left groin lymph nodes was carried out. The surgical margins, and lymph nodes were free of cancer. This tumor is rare, and the histogenesis is uncertain. It occurs most frequently in the limbs of young females, and runs an indolent course but usually results in a lethal outcome. It is recommended that wide local excision and dissection of regional lymph nodes be carried out. Adjuvant systemic chemotherapy and/or immunotherapy for a finite period of time is logical, but appropriate agents have yet to be defined. Local radiation may be indicated for the tumor not amenable to excision with wide free margin. Lifelong follow-up is mandatory based on a propensity for late recurrence. (Author abstract) (41 Refs)

3. NEUROTROPIC MELANOMA OF THE VULVA.

Warner TF, Hafez GR, Buchler DA

Dept. Surgical Pathology, Clinical Sciences Center, Univ. Wisconsin, Madison, WI, 53792

Cancer; 49(5):999-1004 1982

A spindle cell melanoma of the clitoris was associated with a large area of lentiginous melanocytic dysplasia in the vulva of a 51-yr-old woman. There was extensive neoplastic infiltration of the dermis, a desmoplastic reaction, and replacement of perineurial and Schwann cells by tumor cells (neurotropism). The superficial dysplastic components were pigmented, but melanosomes were not identified in a l ymph node metastasis. Here the internuclear areas strongly resembled neuropil. Vulvar melanoma is rare, and this is the first report of neurotropic melanoma in this site. (Author abstract) (21 Refs)

VAGINAL TUMORS

4. LONG-TERM FOLLOW-UP IN RADIATION THERAPY OF CARCINOMA OF THE VAGINA.

Perez CA, Camel HM

Div. Radiation Oncology, Mallinckrodt Inst., 4511 Forest Park, St. Louis, MO, 63108

Cancer; 49(6):1308-1315 1982

A retrospective analysis of 134 patients with histologically confirmed carcinoma of the vagina is reported. Actuarial disease free 5-yr survival was: Stage 0 (15 patients), 90%; I (39 patients), 90%; IIA (39 patients), 58%; IIB (21 patients), 32%; III (12 patients), 40%; IV (8 patients), 0%. Fifteen patients had carcinoma in situ; of these, 14 were controlled with interstitial or intracavitary therapy. Of 39 patients with Stage I carcinoma, 37 (95%) showed no evidence of vaginal or pelvic recurrence. Most of them received interstitial or intracavitary therapy or both; the addition of external beam irradiation did not significantly increase survival or tumor control. In Stage IIA (paravaginal extension) 22 of 34 (64.7%) patients were controlled with a combination of brachytherapy and external beam irradiation; only two of five (40%) treated with brachytherapy alone exhibited tumor control in the pelvis. Eight of 12 Stage III tumors were controlled in the pelvis. Only two of eight patients with Stage IV had no recurrence in the pelvis even with relatively high doses of irradiation. The dose of irradiation delivered to the primary tumor or the parametrial extension was critical in achieving successful results. The incidence of complications (9.7%) is correlated with the stage of the tumor and type of treatment given. (Author abstract) (19 Refs)

CERVICAL AND UTERINE TUMORS

5. CERVICAL CANCER: SURGICAL STAGING TO IMPROVE SURVIVAL.

Averette HE, Buchsbaum HJ, Girtanner RE, Nelson JH, Piver MS

Div. Gynecologic Oncology, Univ. Miami Sch. Medicine, Dept. Obstetrics and Gynecology, Miami, FL

Contemp Obstet Gynecol; 19(2):44-48,51-52,57-63 1982

The value of staging laparotomy to improve survival of patients with cervical cancer was discussed. In the first group of patients with Stages IIb and III disease, 46% of the latter and 16% of the former had positive para-aortic nodes. In a study of 100 consecutive patients, 14% with Stage IIb, 37% with Stage IIIb, and 57% with Stage IVa disease had para-aortic node metastases; overall, 28% had positive nodes. Of 150 patients explored, para-aortic metastases were found in one-third with Stage IIIb disease; 20 patients had visceral metastases. Dissemination throughout the abdomen can be missed with staging methods recommended by the International Federation of Gynecology and Obstetrics. In carefully selected pat ients, the finding of positive nodes in 8% of patients with Stages Ib and IIa cervical cancer led to a change in therapy from radical hysterectomy to extended field pelvic and para-aortic radiotherapy. Surgical staging techniques are described and illustrated and advantages and disadvantages discussed. Of patients with Stages Ib and IIa cervical cancer and positive para-aortic nodes, 41% have survived for 5 yr or more following surgical staging. (8 Refs)

6. THE BASEMENT MEMBRANE IN THE CARCINOMA IN SITU OF THE CERVIX: A MORPHOLOGICAL STUDY.

Minh HN, Smadja A, Lecomte D, Orcel L
Laboratoire d'Anatomie Pathologique, Centre Hospitalier Universitaire, B.P. 3006, 80030 Amiens Cedex, France
Eur J Obstet Gynecol Reprod Biol; 12(6):373-383 1981

The prognostic significance of stroma-invasion potential of carcinoma in situ of the uterine cervix attributed to histologic alterations of the basement membrane was investigated. Sixty-eight cases of carcinoma in situ were examined histologically after punch biopsies. Forty-six cases of undifferentiated carcinoma in situ arising from the squamous-columnar junction were found. Light microscopy revealed an epithelium composed of small tumor cells with disappearance of epithelial stratification and no surface maturation or keratin formation. A continuous and clearly delineated basement membrane parallel to the basal layer was also present. Electron microscopy revealed immature cells of great uniformity with oval nuclei and axis vertical to the basement membrane. Desmosomes were rate and imperfectly differentiated. Twenty-two cases of differentiated carcinoma involved the squamous epithelium of the portio. Epithelial differentiation and stratification were always significantly disturbed and surface keratin formation was sometimes evident. The basement membrane had a fibrillar structure due to irregular reticular fibers. Electron microscopy revealed polygonal shaped cells with individual pleomorphism sometimes evident. Desmosomes were less frequent than in normal squamous epithelium; their processes were shorter and the dense intercellular plaque was usually not evident. Study of the basement membrane is a useful diagnostic criterion for stroma-invasion potential in carcinoma in situ of the cervix. (20 Refs)

7. AN IMMUNOLOGICAL ASSESSMENT IN PATIENTS WITH UTERINE CERVIX CARCINOMA.

Bonnetterre J, Santoro F, Wattre P, Beuscart R, Adenis L, Capron A
Centre Oscar-Lambret, rue Frederic-Combemale, B.P. 307, F 59020 Lille, France
Gynecologie; 32(3):257-266 1981

The relationship between cellular and humoral immunity parameters and stage, treatment and prognosis of cervix cancer was examined in 111 women with carcinoma in situ (12: mean 48.2), Stage I or II neoplasms (57: mean age 52.2), or Stage III or IV neoplasms (42: mean age 62.4). Increased inhibition of phytohemagglutinin (PHA)- or concanavalin A-induced lymphoblastic transformation was evident in more advanced cancers. The percentage and absolute number of T-lymphocytes was identical in the three groups. The percentage of B-lymphocytes was increased in more advanced cancers while the absolute number of B-lymphocytes remained constant. Tuberculin skin tests were positive in 3/7 patients in Group I, 12/32 in Group II, and 8/12 in Group III. Thirty-eight of 93 patients had abnormal levels of circulating immune complexes. The mean plasma carcinoembryonic antigen levels were 8.4, 12.9 and 48.9 nanog/ml for Groups I, II, and III, respectively. No significant difference in IgG and IgM concentrations were observed as a function of group. The mean level of IgA was significantly increased in Group III patients. Complement 3 activity increased with more advanced cancers; complement 4 activity was increased in Group III patients. Various analysis found some associations between clinical and immunological parameters: age of patients, complement factors, and circulating immune complexes; lymphoblastic transformation with mitogens also were closely correlated. Linear regression test demonstrated a relationship between lymphoblastic transformation and skin tests and circulating immune complexes and levels of carcinoembryonic antigen, IgA, IgM, and complement 3. (58 Refs) (In FRE)

8. OUTPATIENT THERAPY: SUCCESS AND FAILURE WITH DYSPLASIA AND CARCINOMA IN SITU.

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Am J Obstet Gynecol; 142(3):323-329 1982

Between 1971 and 1980, 385 patients with colposcopic biopsy-proved cervical intraepithelial neoplasia were treated by either the colposcopist or the referring physician by means of cryosurgery, electrocautery, or biopsy excision. All were observed for a minimum of 1 yr, 220 between 1 and 2 yr, 50 between 3 and 4 yr, and 25 for 4 or more yr. Therapy failed in 29 in the 1st yr ('failures' proved by tissue examination). The failure rate among the 35 patients with carcinoma in situ was 20%, a rate significantly higher than that seen in 108 patients with severe dysplasia (7 or 6.5%) or in mild and moderate dysplasia (4.4% and 8.5%, respectively). There were 10 'recurrences' seen among those observed for more than 1 yr after treatment. In eight instances the histologic severity of the recurrence was more severe than that of the original lesion. The comparative efficacy of cryosurgery and electrocautery and the success and failure rates for the colposcopists and other therapists who had not viewed the lesions prior to therapy are examined. (Author abstract) (12 Refs)

9. SEVERE CERVICAL DYSPLASIA: CONTROL BY BIOPSIES OR PRIMARY CONIZATION? A COMPARATIVE STUDY.

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Acta Obstet Gynecol Scand; 60(6):549-554 1981

During the period 1967-75 severe cervical dysplasia was diagnosed in 87 consecutive cases by means of colposcopically directed biopsies of the portio and by cervical curettage. Thirty-eight of the patients were treated, 3-6 weeks after diagnostic biopsy, by conization (conization group) and subsequently followed with smears and colposcopy. The remaining 49 patients (the biopsy group) were followed up at regular intervals by colposcopically directed biopsies of the portio and cervical curettage. The follow-up period for all 87 patients ranged from 9 to 106 months, mean 47.6 months. The groups were comparable with respect to the most important epidemiological factors. During the follow-up period progression to carcinoma in situ and to microinvasive carcinoma was found in 57.1% of the biopsy group but in 0% of the conization group. Of the whole material, 69 patients had conization (the 38 patients of the conization group plus 31 of the biopsy group). In three cases (4.35%) the cone diagnosis was one grade more serious than the biopsy diagnosis. The mean transit time of progression from severe dysplasia to CIS/MIC was 12-15 months. It is concluded that severe dysplasia is a rapidly progressing state which can be safely diagnosed by colposcopically directed biopsies of the portio and cervical curettage and effectively treated by conization. In view of the fact that not less than 32.7% of the cases with severe dysplasia in the biopsy group regressed during follow-up, we recommend that the diagnosis be established by portio biopsies and cervical curettage, twice, with an interval of 3 months to restrict the number of superfluous conizations. (Author abstract) (15 Refs)

10. PARA-AORTIC LYMPH NODE IRRADIATION IN CARCINOMA OF THE CERVIX AFTER EXPLORATORY LAPAROTOMY AND BIOPSY-PROVEN POSITIVE AORTIC NODES.

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Int J Radiat Oncol Biol Phys; 8(1):13-18 1982

Pelvic and para-aortic lymph node (PALN) radiotherapy (RT) was administered following staging laparotomy in 23 women (34-75 yr old) with positive PALN and cervix neoplasms (18 squamous cell carcinomas, 5 adenocarcinomas). The delay between surgery and start of RT averaged 10 days. Cobalt-60 was used in all patients for external RT of fields including the pelvic, iliac, and para-aortic nodes. A daily tumor dose of 180 rad was delivered to the midplane of the abdomen and pelvis, in 5 daily fractions/wk. The majority of the patients received a total midplane dose ranging from 4,000 to 6,000 rad to the pelvis and from 5,000 to 5,500 rad to the PALN area by external RT. Intracavitary radium was used in the form of two inserts in 15/23 patients and one insert in 5/23. Five patients were alive with no evidence of disease 115, 110, 90, 73, and 45 mo after completion of RT. Three of the five surviving patients developed bowel complications requiring surgery. Fifteen patients died of cancer at an av of 21 mo. The av survival was 40 mo. Of 18 deceased patients, 5 had developed late bowel radiation damage, 3 requiring surgical intervention. Sites of failure were as follows: 5 pelvis, 2 lung, 2 generalized, 2 scalene lymph nodes, 1 lung and bone, 1 bone, 1 anasarca, and 1 unknown. During RT, the main side effects were nausea, vomiting, and diarrhea sufficiently severe in some patients to lead to difficulties in electrolyte balance and nutritional problems. (29 Refs)

11. HIGH VERSUS LOW DOSE-RATE INTRACAVITARY RADIOTHERAPY IN THE TREATMENT OF CARCINOMA OF THE UTERUS. A COMPARATIVE STUDY OF AFTERLOADING CO60 (CATHETRON) AND CONVENTIONAL (RADIUM) TREATMENT.

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Acta Obstet Gynecol Scand [Suppl]; (103):7-27 1981

Afterloading Co60 and conventional radium therapy of carcinoma of the uterus are reviewed, and a comparative study of the two methods is presented. Intracavitary radium therapy of cervical carcinoma is performed by two principle methods. The Paris method uses small amounts of radium over a long period of treatment for a total dose to the paracervical triangle of 72 Gray. The Stockholm method uses larger amounts of radium in a short, intense treatment, for a dose to the cervix, lower uterine segment, vaginal vault, and paracervical triangle of approx 70 Gray. Cancer of the endometrium is treated by the single linear radium source method, Heyman's packing technique, or intracavitary vaginal radium therapy. Afterloading Co60 (Cathetron) therapy employs various catheters into which Co60 is inserted. The appropriate catheters are inserted into the vagina and uterus and are fixed in place using vaginal prostheses. Afterloading therapy and conventional radium therapy were compared in a study of 101 patients with cervical carcinoma and 91 patients with endometrial carcinoma. Conventional therapy had the advantages of long half life, longest clinical experience, and availability of radium sources. Radiation exposure posed a hazard to patients and staff. Cathetron therapy had the advantages of convenience, radiation protection to the staff and other patients, minimization of hospitalization, good fixation of treatment catheters, and the ability to treat many patients per day. (111 Refs)

12. A COMPARISON OF CLINICAL RESULTS FOLLOWING HIGH DOSE-RATE INTRACAVITARY AFTERLOADING IRRADIATION WITH CO60 (CATHETRON) AND CONVENTIONAL RADIUM THERAPY FOR ST. I-II CERVICAL CARCINOMA.

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Acta Obstet Gynecol Scand [Suppl]; (103):31-38 1981

From 1969 to 1976, 101 patients with St Ia-IIb cervical carcinoma were treated with the Cathetron (C) and 84 patients with radium (R). Surgery was carried out on 56.4% of the patients in Group C and 60.7% in Group R 2 wk after the intracavitary radiotherapy and 51.5% of the patients in Group C and 45.2% in Group R received external irradiation with or without an operation. There was no statistical difference in the survival between the two treatment groups, the 5-yr crude survival rate being 81.6% for Group C and 78.6% for Group R and the 3-yr crude survival rates 85.1% and 83.3% respectively. Local recurrence of tumor was more frequent in Group R (10.7%) than in Group C (3.0%) ($p = 0.03$). There were more early complications during or after the Cathetron (10.9%) than radium treatment (3.6%), without any statistical significance, however. No differences were found in operative difficulties or early postoperative morbidity between the two groups during or after radical operations after intracavitary radiotherapy. (Author abstract) (51 Refs)

13. COMPLICATIONS FOLLOWING HIGH AND LOW DOSE-RATE INTRACAVITARY RADIOTHERAPY FOR ST. I-II CERVICAL CARCINOMA: A COMPARISON OF REMOTELY AFTERLOADED CO60 (CATHETRON) AND CONVENTIONAL RADIUM THERAPY.

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Acta Obstet Gynecol Scand [Suppl]; (103):39-49 1981

A study was made to compare the incidence, quality and etiology of complications after low and high dose-rate intracavitary radiotherapy for St Ia-IIb cervical carcinoma in 185 patients, of whom 84 were treated with radium (R) and 101 with afterloaded Co60 (Cathetron, C), from 1969 to 1976. The frequency of surgery and external irradiation was similar in both groups. There were more ($p = 0.01$) complications in Group C (27.7%) than in Group R (13.1%). However, when the single fractions in the Cathetron treatment were lowered from 10 Gy to 7.5 Gy each in 1972, the incidence of complications decreased from 42.4% to 20.6% ($p = 0.02$) and the latter incidence was not statistically different from Group R. Intestinal complications were more frequent than urological ones in both groups. low wt was significantly (p less than 0.025) correlated with the development of complications and previous laparotomy ($p = 0.0001$) with the development of fistulae in Group C. (Author abstract) (57 Refs)

14. RADIATION DOSE CALCULATIONS IN ENDOMETRIAL CANCER TREATED WITH HEYMAN CAPSULES OR TANDEM.

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Gynecol Oncol; 13(1):37-43 1982

The radiation dose calculated when endometrial cancer patients are treated with Heyman capsules in uncertain owing to shielding and irregular placement of sources. When we compared the doses calculated in six patients treated with capsules and tandem, we found in the isthmus that the tandem gave a more uniform and higher dose than the capsules for 5,500 mg-hr. In the body, the capsules give an overall nonuniform and higher dose than the tandem for 5,500 mg-hr. We advise tandem treatment alone for a small uterine cavity. For a large cavity, we recommend tandem treatment combined with capsules, which provides the advantage of uniform dose in body and isthmus with increased dose from the capsules in the body. (Author abstract) (6 Refs)

15. INTRACAVITARY IRRADIATION OF ENDOMETRIAL CARCINOMAS OF THE UTERUS IN STAGE I USING A 'BULB TECHNIQUE': PHYSICAL BASIS.

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Br J Radiol; 55(649):56-59 1982

In an attempt to replace the well-known low dose-rate 226Ra in the Heyman packing method with a high-dose-rate afterloading system (Cathetron with 60Co sources) for the treatment of stage I carcinoma of the uterine body, a new concept called the 'bulb technique' has been developed. Different 60Co source trains have been combined to create isodose curve distributions adjusted to the individual size and form of the uterine body. Computer simulation and measurements were used to establish the physical basis of the technique. (Author abstract) (8 Refs)

16. VALUE OF MULTI-PLANAR CT IMAGES IN INTERACTIVE DOSIMETRY PLANNING OF INTRACAVITARY THERAPY.

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Int J Radiat Oncol Biol Phys; 8(2):295-301 1982

Application of multi-planar reconstructed computed tomography (MPRCT) and specific application to the treatment planning of intracavitary radium therapy (ICRT) for adenocarcinoma of the endometrium (ACE) are discussed. Demonstration case pertains to a 68-yr-old patient whose chief complaints were post-menopausal vaginal spotting for approx 5 mo. Diagnosis and clinical staging were ACE, clinical Stage II, Grade III. Radiation treatment (RT) comprised of whole pelvis external beam irradiation to a midline dose of 4,000/4 wk, followed by ICRT for 72 hr. Computed tomography (CT) scanning of the pelvis was done on whole body scanner prior to RT, during and after ICRT. Transaxial images and radiographic views are shown. Dose rates at estimated representative node-bearing sites from the technique of orthogonal radiographs are compared with the values obtained by the method of using MPRCT images. The differences in dose rates range from 0.1 to 2.5 rad/hr. Results reflect the displacement of the applicator, the more posteriorly location relative to the cervical os and the tandem, and hence closer to the rectum. Small lapses in the proper positioning of the ovoids and inadequate vaginal packing can result in significant increases in the bladder and rectum dose rates. Major advantage of the MPRCT approach is in the display of dose rate distribution on CT images in multiple plains and the method presents substantially more dosimetry information for immediate clinical evaluation. (19 Refs)

17. GASTROINTESTINAL COMPLICATIONS AFTER RADIOTHERAPY FOR CARCINOMA OF THE UTERINE CERVIX.

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Can J Surg; 25(1):64-66 1982

Radiotherapy for invasive carcinoma of the uterine cervix caused gastrointestinal complications in 52 of 441 patients. External beam and intracavitary radiation together caused greater bowel damage than either method alone. Twenty-eight of the 52 patients required surgical intervention. Ileal stenosis in nine patients required primary resection with anastomosis in seven while the stenosis was bypassed in the other two. Acute perforation with peritonitis would require a diverting ileostomy and creation of a mucous fistula. A defunctioning colostomy was indicated for relief of pain, bleeding and stenosis of the rectum in 11 of 15 patients; 2 patients were treated by primary resection, 1 underwent abdominoperineal resection and another a pelvic exenteration. Of four patients with ileal and rectal involvement, one underwent right hemicolectomy and transverse colostomy, two had ileal resection and sigmoid colostomy and the other had hemicolectomy and rectal resection. All patients were well at follow-up from 3 to 120 mo after operation. A Hartmann's procedure is indicated when it appears that primary closure may not succeed. Individualized management is essential. (Author abstract) (13 Refs)

18. THE RISK OF SECOND PRIMARIES SUBSEQUENT TO IRRADIATION FOR CERVIX CANCER.

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Int J Radiat Oncol Biol Phys; 8(2):207-211 1982

The risk of developing a new primary malignancy following radiation therapy (RT), alone or combined with surgery, for invasive cancer of the uterine cervix was studied in 1,048 patients with histologically proven invasive carcinoma Stages I, II, or III, who were followed up with a median period of 4 yr. During the observation time 32 second primaries (SP) were reported. No statistically significant difference between the observed and expected number of SP was noted. Using the person yr approach, the SP incidence rate was 5.49/1,000 person-yr. Eleven SP were observed in the pelvic region: colon, rectu m, endometrium, and vagina, while 20 occurred outside the pelvis. Neither the incidence of pelvic SP nor that of extra-pelvic SP was greater than expected. The time from RT to diagnosis of a SP ranged from 1 to 16 yr with a median of 8 yr for pelvic SP, and 6 yr for extra-pelvic SP. The incidence of SP increased with the stage of cervix cancer; the increase is statistically significant. Mean ages of Stage II and Stage III patients were higher than that of Stage I patients. No significant difference of a possible carcinogenic effect of RT was noted between the patients treated with RT alone (6,000-8,000 rad) and patients treated preoperatively or postoperatively (3,000-5,000 rad). SP had no impact on the survival experi-

ence of the study population in the first 5 yr after treatment; after 5 yr some deaths were observed, but patients are at higher risk of death from other causes than from SP. (15 Refs)

19. SUBSEQUENT MALIGNANCIES ASSOCIATED WITH CARCINOMA OF THE UTERINE CERVIX: INCLUDING AN ANALYSIS OF THE EFFECT OF PATIENT AND TREATMENT PARAMETERS ON INCIDENCE AND SITES OF METACHRONOUS MALIGNANCIES.

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Int J Radiat Oncol Biol Phys; 8(2):197-205 1982

Records of 763 previously untreated patients with invasive carcinoma of the uterine cervix from 1953 to 1972 were reviewed to investigate the occurrence of second malignancies (SM) and to determine the influence of various epidemiological and treatment factors on the development of SM. Eighty eight of the patients (87% white, and 10% black) had squamous cell carcinoma, and 8% adenocarcinoma. Majority of patients (74%) were treated with a combination of radiation therapy, and 93% received irradiation as part of the initial therapy. The follow-up status was known until the time of death or for periods of 5-25 yr in 96% these patients. The overall 5-yr survival for the entire group was 57%. A statistically significant (SS) excess of lung and vulva-vaginal cancer and a SS decrease in breast cancer were noted. No SS increase was seen for any of the 5-yr time periods in development of second primaries at all sites after the initial diagnosis of cervix cancer. A similar calculation for lung cancer and vulva-vaginal cancer is presented. Although the numbers are small, a SS over the expected number of lung cancers was noted in the first 2 yr of the 5-yr interval. A Cox regression analysis demonstrated no significant effects of external beam radiation or radium exposure on the overall incidence of SM controlling for age, race, histology of cervical carcinoma, and stage. (92 Refs)

20. RESULTS OF RADIATION THERAPY GIVEN AFTER RADICAL HYSTERECTOMY.

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Cancer; 49(6):1278-1285 1982

Two hundred twelve patients with carcinoma of the cervix, Stage I (193 patients) and Stage II (19 patients), were treated by radical hysterectomy at the Hospital of the University of Pennsylvania during the period from 1955-1977. Pathology reports were evaluated for the presence of the following factors thought to indicate an unfavorable prognosis: (1) positive pelvic lymph nodes (31 patients); (2) parametrial extension (22 patients); and (3) infiltration of the margin of resection (14 patients). Fifty-one high risk patients (HR) with one or more of these pathologic findings have 5 and 10 yr survivals of 55% and 30%, respectively. This compares with 5-and 10-yr survival of 87% and 85%, respectively, for patients without these findings. Local recurrences were noted in 20/50 (40%) HR patients versus 23/159 (13.2%) non-HR patients (p less than 0.001). A retrospective analysis revealed that 21 of 50 evaluable HR patients received adjunctive postoperative pelvic irradiation (HR-XRT). Although the reduction in local recurrence in the treated group approached statistical significance, 5/21 versus 15/29 (0.1 greater than p greater than 0.05), the 5-and 10-yr survival did not differ significantly. Twenty-four patients initially treated with surgery received definitive radiation therapy for local recurrence. The 5-and 10-yr survivals from the time of recurrence were 22% and 15%. Our findings suggest that postoperative irradiation may be beneficial in controlling local disease in subgroup of radical hysterectomy patients who are at high risk for recurrence. Since the ultimate incidence of extra pelvic metastasis for the high risk and the recurrent group is 32% and 67%, respectively, however, it appears that improved survival awaits the development of effective systemic adjuvant therapy. (Author abstract) (38 Refs)

21. ANALYSIS OF RESIDUAL DISEASE FOLLOWING PREOPERATIVE RADIOTHERAPY VERSUS INITIAL SURGERY IN ENDOMETRIAL CARCINOMA.

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Int J Radiat Oncol Biol Phys; 8(2):213-218 1982

The correlation between the extent and location of residual tumor after pre-operative radiotherapy (RT) and the tumor grade, clinical and surgical stage and prognosis was studied in 107 patients with Stage I and II carcinoma of the endometrium; 67 patients (33 Stage I, 34 Stage II) received preoperative RT followed by surgery, while 40 patients (Stage I) had initial operation followed by postoperative RT. Histological grade and type, incidence of residual disease (RD) after preoperative RT, site of RD, depth of myometrial and vascular invasion, and clinical staging are presented. Seven of 67 patients and 3/40 patients developed recurrences and died of disease. Recurrences and death occurred in 24 mo (80%) in 8 of those 10 patients and all within 48 mo of treatment. In 16% of patients with RD were cancer related deaths compared to none in 22 patients without RD. The incidence of cancer related deaths was significantly higher in patients with extrauterine disease than in those with RD confined to the uterus. In the initial operation group, the frequency of cancer-related death in patients who had uterine disease only vs extrauterine disease were 3 and 50% respectively. Patients with Grade 3 tumors had significantly more RD, extrauterine spread, and cancer-related death compared to those with Grade 1 or 2. No comparable trends with stage of disease were noted. (10 Refs)

22. ENDOMETRIAL CARCINOMA WITH CERVICAL INVOLVEMENT (STAGE II): PROGNOSTIC FACTORS AND VALUE OF COMBINED RADIOLOGICAL-SURGICAL TREATMENT.

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Gynecol Oncol; 13(1):76-86 1982

Tumor infiltration into the cervical mucosa, defined as infiltration into either glandular and/or squamous epithelium and the underlining stroma, could, when reevaluated, be verified in only 96 (56.3%) out of 174 cases originally recorded as Stage II endometrial cancer. The finding of 'free floating tumor cells' in the cervical scraping material was associated with a lower frequency of blood/lymph vessel invasion, and these cases had a prognosis similar to Stage I disease. Poor prognostic factors were grossly invaded cervix, enlarged uterine cavity, deep myometrial infiltration, invasion into endothelial lined spaces, and poorly differentiated tumors. Clear cell carcinomas had significantly poorer prognoses than pure adenocarcinomas. The majority of the patients received preoperative radium packing. Six patients experienced major complications, all occurring in cases treated with a combination of intracavitary radium packing and external irradiation. The complication risk was clearly

related to the irradiation dosage from the radium packing. In the prospective clinical trial 40 cases with Stage II adenocarcinomas receiving 4,000 rad postoperative irradiation to the pelvic lymph nodes (Group B) had a similar 5-yr survival rate (85%) as the 44 cases receiving no external radiotherapy (Group A). Moreover, seven pelvic recurrences were seen in Group B, and only one in Group A (p less than 0.05). No subgroup of patients could be identified for which external radiotherapy improved the outcome. (Author abstract) (10 Refs)

23. A STUDY OF 333 PATIENTS WITH ADENOCARCINOMA OF THE ENDOMETRIUM TREATED BY COMBINED SURGERY AND RADIATION THERAPY (1958-1978).

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Sem Hop Paris; 58(9):539-545 1982

Patient characteristics and combined radiosurgical treatment of women (34-92 yr old; mean age 63 yr) with endometrial cancer (204 Stage I, 40 Stage II, 24 Stage III, and 20 Stage IV) are described. Of the 333 patients, 274 were post-menopausal, 26 peri-menopausal, and 32 were premenopausal. Gynecologic and obstetric antecedents and associated diseases are described. Metrorrhagia was found in 224/333 patients. Hysterographic and lymphographic findings are presented. Of the tumors, 261 were well- and 31 medium-differentiated adenocarcinomas; 23 were totally undifferentiated. Premenopausal women had a better 5-yr survival rate (73.2%) as compared with peri-menopausal (59.9%) and post-menopausal (57.0%) women. The survival rates for patients with Stage I-IV cancers were 67.0%, 60.0%, 32.5%, and 10%, respectively. Survival rates for patients with well-, medium-, and undifferentiated tumors were 64.4%, 52.7%, and 5.9%, respectively. The 5-yr survival rate for 203 patients who underwent radiosurgery was 69.1%; for 35 patients considered inoperable and treated with radiotherapy alone, it was 35.2%. Best results were obtained when preoperative curietherapy, surgery, and postoperative radiotherapy were used (75 patients: 30.2% 5-yr survival rate). Of 45 patients treated for recurrence or metastasis, 35 were treated with surgery alone, 7 with radiotherapy alone, and 3 with radiosurgery. Treatment complications included cystitis (12 patients), simple rectitis (43), and minor accidents (55). Curative and palliative treatment of endometrial cancer is discussed. (11 Refs) (In FRE)

24. CHEMOSENSITIVITY TESTING WITH CIS-PLATINUM(II) DIAMMINEDICHLORIDE. I. A NEW CONCEPT IN THE TREATMENT OF CARCINOMA OF THE CERVIX.

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Gynecol Oncol; 13(1):1-9 1982

A relatively simple, clinically applicable approach for determining the in vivo sensitivity of squamous cell carcinoma of the cervix to cis-platinum(II) diamminedichloride (DDP) is described. Histologic and cytologic characteristics in sequential cervical biopsies were employed to evaluate the sensitivity of tumor to platinum therapy. The remarkable similarity in histologic response of squamous cell carcinoma of the cervix when treated by platinum or radiation therapy suggests that this system might help to identify the patient who would most benefit from systemic platinum chemotherapy, just as it has been useful in identifying patients who can benefit from radiation therapy. (Author abstract) (17 Refs)

25. CHEMOSENSITIVITY TESTING WITH CIS-PLATINUM(II) DIAMMINEDICHLORIDE. II. PRELIMINARY EXPERIENCE IN THE TREATMENT OF CARCINOMA OF THE CERVIX.

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Gynecol Oncol; 13(1):10-18 1982

Nineteen previously untreated patients with invasive squamous cell carcinoma of the cervix were given a test dose of cis-platinum(II) diamminedichloride (DDP) prior to treatment with radiotherapy or initial surgery. Two patients who had failed radiation therapy were also tested. Histologic and cytologic characteristics in sequential cervical biopsies and clinical response were employed to determine sensitivity of tumor to platinum and to identify the patient who would most benefit from systemic platinum chemotherapy. No serious side effects were encountered. Standard treatment could be administered without unexpected toxicities or delay. (Author abstract) (13 Refs)

26. CISPLATIN CHEMOTHERAPY FOR DISSEMINATED ENDOMETRIAL CANCER.

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Obstet Gynecol; 59(2):225-228 1982

Twenty-six women with advanced or recurrent endometrial cancer were treated with cisplatin at a dose of 50, 70, or 100 mg/m2 every 4 wk. An objective response was obtained in 11 of 26 patients (42%), with 10 partial responses and 1 complete response. The median duration of remission was 5 mo, with a range of 2 to 11 mo. The complete response lasted 8 mo. Five patients had stable disease lasting an av of 5 mo. One of 6 patients (16.6%) responded to cisplatin at a dose of 50 mg/m2, 4 of 7 (57%) responded to the dose of 70 mg/m2, and 6 of 13 (46%) responded to the dose of 100 mg/m2, but the differences were not statistically significant ($p = 0.2$). In 8 of 26 cases (31%) cisplatin was discontinued because of toxicity. Three patients developed a peripheral neuropathy, one patient refused further therapy because of vomiting, two patients had nephrotoxicity, and two others had both nephrotoxicity and neurotoxicity. The av total cumulative dose of cisplatin administered when renal deterioration and neuropathy occurred was approximately 500 mg/m2. Cisplatin is definitely active against endometrial cancer, but toxicity precludes it prolonged administration in high doses on an outpatient basis. By maintaining a forced diuresis, toxicity can probably be decreased, thereby permitting continued administration of cisplatin. The drug may also be more useful when used at a lower dose in combination with other active agents against endometrial cancer. (Author abstract) (10 Refs)

27. ADJUVANT GESTAGEN THERAPY OF ENDOMETRIAL CARCINOMA.

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Zentralbl Gynaekol; 103(21):1289-1293 1981

Reference is made in this paper to histological findings, with the view to presenting the results of preoperative gestagen therapy, using hydroxyprogesterone capronate, applied to 334 patients with endometrial carcinomas. Complete tumor regression was achieved in 8.7% of these cases. Further differentiation and increased secretion of the tumor cell were recorded in 56.6%. No gestagen effect at all was recordable from 34.7% only. Sensitivity of endometrial carcinomas to gestagens was at its highest in cases of highly differentiated adenocarcinomas, in premenopausal women, in the presence of estrogenic colpocytological reaction, and when endometrial carcinomas coincided with adipositas and diabetes mellitus. Five-yr survival rates, following surgery in combination with hormonal therapy, reached 91.3% and thus were in excess of the 78.6% recorded from patients with surgical treatment alone. (Author abstract) (3 Refs) (In GER)

28. ENDOMETRIAL CARCINOMA INSENSITIVE TO PROGESTIN AND CYTOTOXIC CHEMOTHERAPY MAY RESPOND TO TAMOXIFEN.

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Acta Obstet Gynecol Scand; 60(6):589-590 1981

Estrogen and progestin receptor-positive endometrial carcinoma, which did not respond with remission to progestin or cytotoxic combination chemotherapy, was sensitive to tamoxifen. This was demonstrated by the complete resolution of pulmonary metastases and pleural effusion, a marked decrease in ESR, and improvement in the general condition of our patient. Although it is very likely that progestin and antiestrogen therapies operate by similar molecular mechanisms, they may be complementary. (Author abstract) (6 Refs)

29. LOWER RELAPSE RATES AFTER NEIGHBOURHOOD INJECTION OF CORYNEBACTERIUM PARVUM IN OPERABLE CERVIX CARCINOMA.

Mignot MH, Lens JW, Drexhage HA, Von Blomberg BM, Flier VD, Oort J, Stolk JG
Dept. Obstetrics and Gynecology, Free Univ. Hosp., Amsterdam, The Netherlands
Br J Cancer; 44(6):856-862 1981

The effect of adjuvant immunotherapy with a single neighborhood injection of 2 mg C parvum (CP) was investigated in a randomized study involving 43 patients with carcinoma of the cervix uteri, all of whom were treated by radical surgery. All patients had carcinoma confined to the cervix, the upper part of the vagina or the parametrial region. When the malignancy had spread to the parametrial region, additional postoperative radiotherapy was given. Twenty two patients received immunotherapy 10 days before surgery, whereas the remaining 21 control patients received no immune stimulation. Only minor side effects of CP were encountered. Follow-up shows a relapse rate of 5% in the CP treated group and of 29% in the controls (p less than 0.05). A further 15 patients with more advanced malignancies were added to our studies. In these, CP stimulation had no effect on relapse rates, but the relapse-free intervals were longer after immune stimulation: control 3.5 mo (mean) -1.5 (sd), CP 13.0 mo -7.0 (p less than 0.05). The number of peripheral T cells and the ability to become sensitized to DNCB were increased after CP stimulation. A decrease was found in the number of blood monocytes and the number of monocytes capable of transforming into active macrophages, indicating a possible sequestration of these cells in the tissues. (Author abstract) (40 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

30. REAL-TIME ULTRASONOGRAPHY FOR DETERMINATION OF OVARIAN MORPHOLOGY AND VOLUME. A POSSIBLE EARLY SCREENING TEST FOR OVARIAN CANCER?

Campbell S, Goswamy R, Goessens L, Whitehead M
(c/o Whitehead) Dept. Obstetrics and Gynaecology, King's Coll. Hosp. Medical Sch., Denmark Hill, London SE5 8RX, England
Lancet; 1(8269):425-426 1982

The accuracy with which ovarian morphology and size can be determined by a real-time, ultrasound mechanical sector scanner was assessed. Both ovaries of 11 climacteric women appeared morphologically normal by ultrasonography and these findings were confirmed at laparotomy the following day. The correlation coefficient between ovarian volumes determined by sonar and those obtained by direct measurement at operation was 0.97. In a series of 31 postmenopausal women in whom clinical examination was unremarkable, both ovaries were identified by sonar in 26 subjects (84%) and a cystic ovary was diagnosed in 1 patient. Ovarian morphology in the other 25 subjects appeared normal and the range of volumes was from 1.47 to 10.43 cm3 with an arithmetic mean of 4.33 cm3 -1.91 (SD). The mean difference between the volumes of the right and left ovaries was 1.48 cm3 -1.19 and the percentage mean difference was 42.88% -32.05. An ovary with a volume more than twice that of the overall mean and also more than twice the size of its fellow should be regarded with some suspicion because ovarian volumes within individuals are clearly related (correlation coefficient = 0.82). The potential of the technique as a screening test for the early detection of ovarian cancer warrants further evaluation. (Author abstract) (5 Refs)

31. EARLY DIAGNOSIS OF OVARIAN CANCER.

Piver MS
Dept. Gynecologic Oncology, Roswell Park Memorial Inst., Buffalo, NY
Hosp Med; 18(1):43-47,50-52 1982

Ovarian cancer is not easily detected by physical or laboratory examination and is not associated with significant symptoms in the early stages. It is the leading cause of death from gynecologic neoplasms; 70% of women present with metastasis beyond the pelvis. Early diagnosis of ovarian cancer requires a higher index of suspicion on the part of physicians, careful examination of all women with vague pelvic and abdominal symptoms, routine pelvic examination at the time of general examination, refinement of the technology of noninvasive tests for detecting pelvic masses, development of a serum immunologic test specific for early-stage ovarian cancer, and careful evaluation for occult metastasis when a clinically 'localized' tumor is found. The most common presenting symptoms include abdominal pain, increasing abdominal girth, bloating, nonspecific digestive abnormalities, pelvic discomfort, and ab-

normal uterine bleeding. Pelvic examination, diagnostic tests, preoperative workup, restaging at laparotomy, and tumor markers are discussed. (16 Refs)

32. ESTROGEN RECEPTORS IN OVARIAN EPITHELIAL CARCINOMA.

Schwartz PE, LiVolsi VA, Hildreth N, Maclusky NJ, Naftolin FN, Eisenfeld AJ
Div. Gynecologic Oncology, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT, 06510
Obstet Gynecol; 59(2):229-238 1982

Specimens from 53% (16 of 30) of patients with untreated ovarian epithelial cancers between October 1976 and February 1979 had estrogen binding levels greater than 30 fmoles/mg of cytosol protein (receptor rich). The likelihood of a specimen being receptor rich appeared to be independent of patient age, histologic grade of tumor, clinical stage, and amount of residual tumor left after surgery. For 20 patients with previously untreated advanced disease a life-table analysis showed no significant difference when receptor-rich and -poor groups were compared in terms of either survival or time to first progression of disease. Analysis of more recent specimens (predominantly obtained after February 1979) indicates high-affinity binding of the estrogen consistent with receptor; occasional substantial heterogeneity in estrogen binding results between different sites of tumor involvement; and progestin-specific binding in some specimens. In an analogy to breast cancer, patients whose tumors are cytosol estrogen receptor rich might theoretically be responsive to the administration of antiestrogens. (Author abstract) (19 Refs)

33. OVARIAN GERMINOMA (DYSGERMINOMA) WITH ELEVATED SERUM LACTIC DEHYDROGENASE: CASE REPORT AND REVIEW OF LITERATURE.

Sheiko MC, Hart WR
(c/o Hart) Dept. Pathology, Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH, 44106
Cancer; 49(5):994-998 1982

Lactic dehydrogenase (LDH) is a glycolytic enzyme that may be elevated in the serum of patients with gonadal and extragonadal germinomas. In this report, the authors describe a young woman with a unilateral ovarian pure germinoma (dysgerminoma) who had greater than a sixfold elevation of serum LDH levels with increases in LDH isoenzymes 1, 2 and 3. Two wk after operation, the serum LDH level had returned to normal. Four additional examples of ovarian germinoma with elevated serum LDH levels have bee n recorded in the literature. The germinoma cells are the likely source of the elevated LDH activity in such cases. Lactic dehydrogenase and its isoenzymes may serve as a useful tumor marker for diagnosis and posttherapy surveillance in patients with germinomas (dysgerminomas, seminomas). The association of elevated serum LDH in patients with other neoplasms is also reviewed. (Author abstract) (28 Refs)

34. LOWER URINARY TRACT RESECTION AS PART OF CYTOREDUCTIVE SURGERY FOR OVARIAN CANCER.

Berek JS, Hacker NF, Lagasse LD, Leuchter RS
Div. Gynecologic Oncology, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
Gynecol Oncol; 13(1):87-92 1982

Twenty-four patients underwent lower urinary tract resection as part of cytoreductive surgery for ovarian epithelial malignancy from 1960 to 1979. Eight patients had partial cystectomies, 2 of which had reimplantation of the ureters, and 16 had partial ureteral resection. Optimal cytoreduction was associated with a longer mean survival. Patients who presented without ureteral obstruction also survived significantly longer than those with obstruction. Morbidity from surgery involving the urinary tract was not excessive in this series. Partial lower urinary tract resection appears justified as part of a primary cytoreductive effort. (Author abstract) (17 Refs)

35. CURRENT CONCEPTS IN CANCER: OVARY - MANAGEMENT OF STAGE I AND II DISEASE. OPTIMAL SURGICAL THERAPY IN STAGE I AND II OVARIAN MALIGNANCIES.

Piver MS
Dept. Gynecologic Oncology, Roswell Park Memorial Inst., State Univ. New York at Buffalo, Buffalo, NY, 14263
Int J Radiat Oncol Biol Phys; 8(2):247-249 1982

Optimal surgical treatment in clinical Stage IA, IB, and Stage II of ovarian cancer is discussed. Conservative unilateral salpingo-oophorectomy (SOE) in Stage IA young patients and bilateral SOE plus hysterectomy in Stage I and II are presented. Conservative unilateral SOE for Stage IA dysgerminomas without postoperative radiation therapy is associated w[illegible] a recurrence rate of approx 25%, and requires careful surgical staging to be certain that occult or subclinical metastases are not present. Since unilateral borderline carcinomas have an approx 100% survival rate, SOE without adjuvant therapy is optimal treatment for those patients desiring to retain future child-bearing capacities. Optimal surgical therapy requires bilateral SOE and hysterectomy plus surgical staging to detect occult or subclinical metastases for Stage I and II. Reviewing women with Stage I and II ovarian cancer, 11% of the Stage I and 23% of Stage II patients had unsuspected diaphragm metastasis; 10% of Stage I and 10% Stage II had subclinical metastasis to para-aortic lymph nodes; 33% of Stage I and 13% of Stage II had positive cytological washings; and 3% of Stage I and none of Stage II patients had metastasis to the omentum. In a simila r study 24% of patients thought to be free of disease at initial surgery had residual disease at restaging laparotomy. Therefore, on discovery of a clinical Stage I or II ovarian carcinoma, the incision should be extended above the umbilicus to enable the inspection of diaphragm and remove the omentum from the transverse colon. (12 Refs)

36. THE ROLE OF POSTOPERATIVE LOCAL OR REGIONAL IRRADIATION IN THE TREATMENT OF STAGE I OVARIAN CANCER.

Powlis WD, Mauch P, Ehrmann RL, Rose CM, Knapp RC, Bloomer WD
Royal Victoria Hosp., 687 Quest Avenue des Pins, Montreal H3A 1A1, Quebec, Canada
Radiology; 142(3):747-750 1982

Histological grade and cell type were major prognostic factors in a retrospective study of 63 patients with Stage I epithelial carcinoma of the ovary. Grading by architectural pattern seemed to predict relapse better than cytological grading. With serous, mucinous, and endometrioid cystadenocarcinomas, relapses increased with higher grades. Relapse oc curred in none of 18 tumors of borderline malignancy, 2 of 27 (7%) with Grade I or II tumor, and 4 of 6 (67%) with Grade III. The upper abdomen and pelvis were both at risk. Because most recurrences were limited to the peritoneal surface in Grade III serous, mucinous, and endometrioid carcinoma, local and regional radiation therapy are justified; postoperative therapy is

not recommended for borderline or Grade I tumors unless ascites or cytological evidence of peritoneal disease is present. Clear-cell carcinoma was uncommon and unfavorable; of 12 cases, 5 involved relapse, with 3 recurrences developing outside the abdomen. (Author abstract) (33 Refs)

37. FQC COMBINATION CHEMOTHERAPY FOR PRIMARY MALIGNANT OVARIAN TUMOR.

Yajima A, Mori T, Wakisaka T, Sato S, Sakahira H, Yamanchi R, Suzuki M
Dept. Obstetrics and Gynecology, Tohoku Univ. Sch. Medicine, Sendai, Japan
Gynecol Oncol; 13(1):93-100 1982

In 111 cases of primary malignant ovarian tumor, laparotomy and surgical resection of the lesion were attempted and all patients then underwent FQC (N1-(2'-tetrahydrofuryl)-5-fluorouracil, carbazilquinone and cytosine arabinoside) combination chemotherapy. Apparently complete resection was obtained in 45 cases (40.5%). The 5-yr relative survival rate was 86.2% in this group. Among the 66 incomplete resection cases, the antitumor response rate of FQC chemotherapy was 48.5% (32 cases). The 4-yr relative survival rate of these cases was 21.4% and their median survival time was 16.2 mo. In contrast, the 4-yr relative survival rate among the nonresponders was 3.8% and their median survival time was 8.7 mo. The results of FQC chemotherapy according to histological type showed relatively good results in cases of mucinous cystadenocarcinoma and endometrioid cystadenocarcinoma, but poorer results in cases of mesonephroid cystadenocarcinoma and embryonal carcinoma. (Author abstract) (33 Refs)

38. CHEMOTHERAPY OF OVARIAN CARCINOMA.

Hogan WM, Young RC
Medicine Branch, NCI, NIH, Bethesda, MD
Cancer- Achievements, Challenges, and Prospects for the 1980s, Proceedings of an International Conference held in New York, 14-16 September, 1980. Vol. 2, Memorial Sloan-Kettering Cancer Center New York, NY. Burchenal, J. H. and Oettgen, H. F., eds. (New York, Grune and Stratton), 944 pp., 1981.

Recent developments in chemotherapy for ovarian cancer are reviewed. The optimal treatment for early stage (I and II) other than Ia(i) and Ib(i) disease remains undetermined. Single alkylating agent chemotherapy has been the most widely used treatment for patients with stages III and IV disease, although recent success with other drugs has been reported. Malignant tumors derived from ovarian germ cells, such as dysgerminoma, endodermal sinus or yolk sac tumor, malignant teratoma, and choriocarcinoma, are discussed. Current investigations emphasize cell culture and clinical pharmacology. (56 Refs)

39. CURRENT CONCEPTS IN CANCER: OVARY - MANAGEMENT OF STAGE I AND II DISEASE. THE PLACE OF ADJUVANT CHEMOTHERAPY IN EARLY STAGES.

Einhorn N
Dept. Gynecological Oncology, Radiumhemmet, Karolinska Hosp. and Inst., S-104 01 Stockholm, Sweden
Int J Radiat Oncol Biol Phys; 8(2):257-258 1982

Problems and role of adjuvant chemotherapy (ACT) in early stages of ovarian cancer (OC) are discussed. In a large patient series, the 5-yr survival rate in serous OC treated between 1958 and 1973 was 71% in Stage Ia and Ib. For mucinous OC, the corresponding rate was 86% and for the endometrioid and mesonephroid types the respective rates were 81% and 70%. The same series contained 1,907 serous OC altogether, 24% were Stage Ia or Ib, as compared with 53% of the mucinous carcinomas, 41% of the endometrioid, 52% of the mesonephroid, and 11% of anaplastic tumors. Considering the hazards of ACT, early-stage mucinous and endometrioid OC without ascites of high differentiation grade should not be admitted to trials that include ACT. The focus of ACT should be the serous and anaplastic varieties and the poorly differentiated tumors of other histological types. Serous-papillary OC of early stages have been allocated to ACT only, chemotherapy only, or low abdominal irradiation followed by chemotherapy. Recent analysis indicate that ACT gives the lowest cumulative 5-yr survival rate (68%), while for irradiation the 5-yr survival rate is 88%, and in the irradiation-chemotherapy group 91%. Contradictions between reports emphasize the need for clinical trials in which due consideration is given to the grade and histologic type, and to improved staging technique and more concordant matching, which includes patient age and time at risk since diagnosis . (13 Refs)

40. SURVIVAL AFTER OVARIAN CANCER INDUCED INTESTINAL OBSTRUCTION.

Piver MS, Barlow JJ, Lele SB, Frank A
Dept. Gynecologic Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263
Gynecol Oncol; 13(1):44-49 1982

Over a 9-yr period, July 1, 1971, to June 30, 1980, 60 women with ovarian cancer underwent exploratory laparotomy for intestinal obstruction secondary to ovarian carcinoma. Surgery consisted of enterocolon bypass (23), ileostomy (9), small intestinal resection (3), colostomy (14), and exploratory laparotomy only in 11 women. In these 11 cases corrective surgery could not be carried out because of extensive tumor. The median survival for the 60 women was only 2.5 mo (less than 1-27) and did not differ significantly for the type of surgery performed: small intestinal bypass, 4 mo (less than 1-15); ileostomy, 2 mo (less than 1-27); small intestinal resection, 1 mo (less than 1-2), colostomy 2.5 mo (less than 1-16); and exploratory laparotomy, 2 mo (less than 1-10). Of the 44 women who received postoperative chemotherapy, 17% (9) had a partial response or stabilization of their disease. Survival was primarily related to the lack of progression of disease after postoperative chemotherapy rather than the type of surgery performed. Patients with a partial response or stabilization of their disease by postoperative chemotherapy had a median survival of 10 mo (4-27) as compared to only 3 mo (less than 1-10) for women with progressive cancer. The recent development of highly active combination chemotherapy which includes cis-dichlorodiammine platinum should lead to improved survival for patients with ovarian cancer induced intestinal obstruction as compared to the poor survival documented for the past decade. (Author abstract) (3 Refs)

41. CURRENT CONCEPTS IN CANCER: OVARY - MANAGEMENT OF STAGE I AND II DISEASE. NEW IMMUNOTHERAPEUTIC AND DIAGNOSTIC APPROACHES TO OVARIAN CANCER.

Order SE, Klein JL, Torres JP
Dept. Radiation Oncology, Johns Hopkins Comprehensive Cancer Center, Baltimore, MD, 21205
Int J Radiat Oncol Biol Phys; 8(2):259-261 1982

Dissemination, staging, prognostic factors, and the biological characteristics of the ovarian cancer (OC) cell are evaluated according to the aspects of new immunotherapeutic and diagnostic approaches to OC. Clinical OC which migrates through

the diaphragmatic lymphatics and into general circulation, does not yield the expected number of disseminated metastases that occur with other cancers. Evaluation of the peritoneal cavity for biomarkers in establishing diagnosis and in determining tumor cell persistence after treatment are possibilities for future clinical programs. The use of immuno-specific antibody will also probably find a role in actual therapy. Alpha and beta globulins associated with OC have been id entified. Tumor associated antigens (TAA) are normal tissue proteins increased in concentration as a result of cancer. TAA may be bound by antibody at tumor sites even if the antigen is present in other normal tissues. Exposing the TAA first to tumor, allows for tumor binding prior to potential binding in other sites bearing the same antigen. TAA appear to be in significantly greater concentration than so called tumor specific antigens. Antiserum to TAA when administered ip in an experimental OC was curative. Cure was achieved by inducing macrophage reactivity against tumor cells. Both TAA and tumor specific antibodies may be used as immune direct binding agents, and contribute to increased cure rate. (20 Refs)

42. PRIMARY OVARIAN LYMPHOMA ASSOCIATED WITH MEIGS' SYNDROME. A CASE REPORT.

Yutani C, Maeda H, Nakajima T, Takeuchi N, Kimura M, Kitamura H
Dept. Pathology, Natl. Cardiovascular Center, 5-125 Fujishirodai Suita, Osaka 565, Japan
Acta Cytol (Baltimore); 26(1):44-48 1982

A case is presented of primary undifferentiated lymphocytic lymphoma, non-Burkitt, of the right ovary associated with Meigs' syndrome. The diagnosis was based upon the findings of tumor imprint cytology, histopathology and electron microscopy. The ultrastructural observations were the most diagnostic, revealing well-developed, rough endoplasmic reticulum and dilated cisternae in the cytoplasm of the tumor cells. An association of Meigs' syndrome with a rare ovarian lymphoma has not been previously reported. The abnormal-appearing mesothelial cells in the pleural effusion were proven to be reactive and not malignant by comparison with the tumor cells demonstrated by imprint cytology of this ovarian lymphoma. (Author abstract) (11 Refs)

43. FAMILIAL OVARIAN CANCER: EIGHT MORE FAMILIES.

Franceschi S, La Vecchia C, Mangioni C
Instituto di Ricerche Farmacologische 'Mario Negri', Via Eritrea, 62-20157 Milan, Italy
Gynecol Oncol; 13(1):31-36 1982

Eight families with multiple occurrence of epithelial ovarian cancer (22 cases) are described. A high proportion of serous and undifferentiated carcinoma, bilateral ovarian involvement, multiple primary cancers, and unfavorable prognosis was found, in agreement with reports concerning 28 previously described families. The importance of family history evaluation and the utility of prophylactic oophorectomy in women from high-risk families are stressed. (Author abstract) (10 Refs)

44. LEUKEMIC INVOLVEMENT OF THE OVARIES IN CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA.

Zarrouk SO, Kim TH, Hargreaves HK, Ragab AH
(c/o Ragab) Dept. Pediatrics, Emory Univ. Sch. Medicine, 1365 Clifton Road NE, Atlanta, GA, 30322
J Pediatr; 100(3):422-424 1982

As children with acute lymphocytic leukemia survive longer, leukemic involvement of the testes is being recognized more frequently and testicular biopsy, even in asymptomatic patients, is being performed on a routine basis. However, leukemic involvement of the ovaries has received little attention, and the significance of ovarian-associated relapse in relation to the eventual outcome of the patient has not been investigated. We describe two female patients with ALL who completed three years of chemotherapy. Both developed ovarian-related relapses after cessation of therapy. (Author abstract) (11 Refs)

TROPHOBLASTIC DISEASE

45. THE BIOCHEMICAL PROPERTIES OF URINARY HUMAN CHORIONIC GONADOTROPIN FROM THE PATIENTS WITH TROPHOBLASTIC DISEASES.

Nishimura R, Endo Y, Tanabe K, Ashitaka Y, Tojo S
Dept. Obstetrics and Gynecology, Kobe Univ. Sch. Medicine, Kobe 650, Japan
J Endocrinol Invest; 4(3):349-358 1981

Human chorionic gonadotropin (hCG) was extracted from urine of a 23-yr-old woman with a hydatidiform mole, a 37-yr-old woman with metastatic choriocarcinoma, and a woman with a normal pregnancy by the standard kaolin-acetate method in conjunction with alcohol precipitation. Purification by diethylaminoethyl-cellulose chromatography and Sephadex G-100 gel filtration was followed by determination of amino acids, carbohydrates, and monosaccharides, sodium dodecyl sulfate polyacrylamide gel electrophoresis, 125I-hCG radioimmunoassay, 125I-hCG uptake in rats, and bioassay by ovarian wt method. Amino acid compositions of the three hCG samples were virtually identical. All three types of hCG could be separated into alpha and beta components by electrophoresis. They were similar in cross reactivities in terms of parallel dose response and dose inhibition to each other in hCG, alpha, and beta-subunits radioimmunoassays. The sialic acid content of hCG from the choriocarcinoma patient was undetectable, whereas the other two hCGs had about 8.5% sialic acid. Ovarian uptake of 125-hCG from the choriocarcinoma patient was approx 10% of the uptakes of the other two 125-hCG types, and agrees with low biological activity determined by the rat ovarian wt assay. Neoplastic or malignant transformation of trophoblasts may alter glycosylation, especially sialylation. (46 Refs)

46. CHEMOTHERAPY WITH THE MODIFIED BAGSHAWE PROTOCOL FOR POOR PROGNOSIS METASTATIC TROPHOBLASTIC DISEASE.

Weed JC, Barnard DE, Currie JL, Clayton LA, Hammond CB
Duke Medical Center, Box 3079, Durham, NC, 27710
Obstet Gynecol; 59(3):377-380 1982

The Southeastern Regional Trophoblastic Disease Center has treated 126 patients with metastatic gestational trophoblastic disease from 1966 through 1979. Sixty-three cases were categorized as having a poor prognosis on the basis of criteria published previously. Since 1976, 18 patients have been treated with a modification of Bagshawe's multiagent chemotherapy protocol. Ten of 18 patients (56%) have achieved sustained remission. Seventy-eight percent of these patients encountered serious myelosuppression (white blood count 1,000 cells or fewer) and 39% suffered severe thrombocytopenia (platelet count 50,000 or fewer). There were no deaths related to drug toxicity. The courses of therapy and complications of modified

Bagshawe chemotherapy are reviewed. (Author abstract) (4 Refs)

MULTI-SITE STUDIES AND REVIEWS

47. THE EFFICACY OF RADIONUCLIDE LIVER AND BONE SCANS IN THE EVALUATION OF GYNECOLOGIC CANCERS.

Harbert JC, Rocha L, Smith FP, Delgado G
Div. Nuclear Medicine, Georgetown Univ. Hosp., 3800 Reservoir Rd., N.W., Washington, D.C., 20007
Cancer; 49(5):1040-1042 1982

Between 1978 and 1980, 33 patients with cervical cancer, 40 patiens with ovarian cancer, and 28 patients with uterine cancer underwent clinical diagnostic staging. Fifty-four patients had bone scans, and 101 patients received liver scans as a part of their staging work-up. No positive bone scan results were found. Eight of 33 patients with Stage IV disease had positive liver scan results consistent with hepatic metastases. Only 1 of 69 patients with Stage I-III disease had a positive test for metastases. While these numbers are small, the authors conclude that bone and liver scanning in asymptomatic patients with early stage gynecologic cancers may not be warranted as staging procedures. (Author abstract) (14 Refs)

48. ANGIOSARCOMAS OF THE UTERUS AND OVARY: CLINICOPATHOLOGIC REPORT.

Ongkasuwan C, Taylor JE, Tang CK, Prempree T
Dept. Radiation Therapy, Univ. Maryland Hosp., 22 S. Greene St., Baltimore, MD, 21201
Cancer; 49(7):1469-1475 1982

The clinicopathologic features of angiosarcomas of the uterus and ovary are described. Extensive review of world literature shows only eight reported cases of angiosarcoma arising in the uterus and two in the ovary. Clinically, both patients presented with nonspecific symptoms. The tumors were found at surgery, and confirmed as angiosarcomas on histologic examination. The ultrastructure of both tumors is also presented. The association with mucinous cystadenoma in the second tumor raises the possibility that this may be a mixed Mullerian tumor. Both tumors behaved in an aggressive fashion. (Author abstract) (15 Refs)

49. TWO YEARS OF CO2 LASER THERAPY: A REPORT OF EXPERIENCES.

Heinzl S
Dysplasiesprechstunde, Universitats-Frauenklinik, Kantonsspital, Schanzenstrasse 46, CH-4031 Basel, Switzerland
Gynaekol Rundsch; 21(Suppl3):45-47 1981

Clinical experiences with laser therapy (LT) of gynecological neoplasms are described. A total of 373 cases treated with LT included: benign alterations of the vaginal part of the cervix (28), cervical intraepithelial neoplasia (163), intraepithelial neoplasia of the vagina (9), intraepithelial ne oplasia of the vulva (6), small carcinomas of the vulva (and recurrences) (4), condylomata acuminata (109), and other conditions (53). LT should be performed shortly after menstruation, when pregnancy can be ruled out and cervical mucus is minimal. LT should not be performed when inflammation of the cervix is found, since the risk of hemorrhage is greater. LT requires a laser with colposcope and smoke-removal apparatus. Energy should be limited to 20 watts. Higher energy may cause abdominal pain and should be used only in rare cases of strong hemorrhage. A minimum destructive depth of 7 mm is required to destroy all involved cervical glands. Of 163 patients treated with LT, 125 were evaluated. Of these, 15 had persistent dysplasia after one treatment; 5 had persistent dysplasia after two treatments. Observation times of 2 yr or less prevented drawing a conclusion about the curative value of LT. (2 Refs) (In GER)

50. BACTERIURIA IN CLOSED BLADDER DRAINAGE VERSUS CONTINUOUS IRRIGATION IN PATIENTS UNDERGOING INTRACAVITARY RADIUM FOR TREATMENT OF GYNECOLOGIC CANCER.

Savage JE, Phillips B, Lifshitz S, Petzold CR, Buchsbaum HJ, Larsen B, Galask RP
Dept. Obstetrics and Gynecology, Univ. Iowa, Iowa City, IA, 52242
Gynecol Oncol; 13(1):26-30 1982

A randomized evaluation of the risk of developing bacteriuria in catheterized patients undergoing their first intracavitary radium insertion for treatment of gynecologic cancer showed no significant difference in bacteriuria when catheter management by continuous neosporin bladder irrigation was compared to closed catheter drainage. This latter method of catheter bladder drainage was simpler to manage and required less nursing and pharmacy support with a smaller cost to the patient. (Author abstract) (7 Refs)

51. COMBINED THERAPY AS AN ALTERNATIVE TO EXENTERATION FOR LOCALLY ADVANCED VULVO-VAGINAL CANCER: RATIONALE AND RESULTS.

Boronow RC
Univ. Mississippi Medical Center, Jackson, MS, 39216
Cancer; 49(6):1085-1091 1982

Locally advanced vulvo-vaginal cancer is a difficult therapeutic problem complicated by the fact that it is an uncommon clinical entity. Surgery for the vulvar (external genital) phase of this disease presentation was combined with radiotherapy for the internal genital phase (with adequate overlap of fields to protect surgical margins). The rationale is that this approach treats the cancer and its dual regional spread patterns, while at the same time preserves the bladder and/or rectum, and should be associated with less morbidity and mortality than exenterative surgery, especially in this predominantly geriatric patient population. During the period from 1968-1980, 33 cancers have been treated. There were 26 primary and 7 recurrent cases. The apparent advantages of this combined therapeutic approach over exenterative surgery include bladder and/or rectal preservation, low primary mortality, low treatment morbidity, and good results in cancer control. (Author abstract) (6 Refs)

52. PRELEUKEMIC GRANULOCYTIC SARCOMA OF CERVIX AND VAGINA. INITIAL MANIFESTATION BY CYTOLOGY.

Spahr J, Behm FG, Schneider V
(c/o Schneider) Dept. Pathology, Medical Coll. Virginia, Box 453, Richmond, VA, 23298
Acta Cytol (Baltimore); 26(1):55-60 1982

Granulocytic sarcoma is an unusual form of tumefaction caused by acute granulocytic leukemia. On rare occasions, the lesion precedes the leukemic phase and presents as a mass with a normal peripheral white cell count. This report describes the initial manifestation of granulocytic sarcoma by vaginal cytol-

ogy in a 39-yr-old female with Down's syndrome. Six days after admission, the patient died of acute peritonitis following spontaneous perforation of the bowel. Autopsy revealed involvement of cervix, vagina, bowel wall and one pelvic lymph node by granulocytic sarcoma. Bone marrow examination confirmed the preleukemic stage of the disease. (Author abstract) (27 Refs)

SELECTED PRE-CLINICAL STUDIES

53. EXPERIMENTAL AND CLINICAL POSSIBILITIES OF XENOTRANSPLANTATION OF GYNECOLOGICAL CARCINOMAS IN THE ATHYMIC NU/NU MOUSE.

Kleine W, Gunther M, Schulze J, Pfleiderer A
Universitats-Frauenklinik, Hugstetterstrasse 55, D-7800 Freiburg i. Br., W. Germany
Gynaekol Rundsch; 21(Suppl3):52-54 1981

Tissue samples from greater than 300 female genital tumors were transplanted into nu/nu mice. Of these, 164 were evaluated, including 80 ovarian, 36 endometrial, 27 cervical, and 21 mammary carcinomas. Growth of transplants was observed for 90% of ovarian, 80% of endometrial, 85% of cervical, and 86% of mammary tumors. Although the overall extent of growth did not differ significantly among tumor types, the speed of growth reflected the type of tumor. Tumor transplants that attained a surface area of 20 square mm within 12 wk were deemed suitable for experimental work. More than 50% of ovarian and cervical carcinomas attained this growth. Only 4/21 transplanted mammary carcinomas reached a size suitable for experimental work. Results indicate that human tumors that proliferate rapidly, such as most ovarian carcinomas, grow rapidly as xenotransplants in nu/nu mice; tumors that grow slowly in humans grow slowly as xenotransplants. Xenotransplants can thus be used as a prognostic indicator. Xenotransplants provide an experimental model intermediate between cell cultures and in vivo tumor in patients. Although drawing correlations between humans and mice is difficult, xenotransplants should be useful for individualization of prognosis and therapy. (no Refs) (In GER)

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Diagnosis, Treatment

SERIES CT17 No. 82/08

AUGUST, 1982

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VULVAR TUMORS

1. INVASIVE SQUAMOUS CARCINOMA OF THE VULVA IN YOUNG PATIENTS.

Choo YC

Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. Michigan Hosp., Ann Arbor, MI, 48109

Gynecol Oncol; 13(2):158-164 1982

Over a 30-yr period, 17 patients below the age of 35 with invasive squamous carcinoma of the vulva were identified, 8 of whom (47.1%) had 'microinvasive' disease. Venereal diseases and condyloma acuminata were not predisposing factors. Immunosuppression was a contributory factor in two patients. Although carcinoma in situ was antecedent in only one patient, it was an associated lesion in 87.5% of patients with 'microinvasive' and 22.2% of patients with invasive carcinoma. The nature and course of this disease in young patients do not differ from the elder counterpart. Prolonged follow-up of these patients has revealed increased susceptibility of the perineum, vagina, and cervix to multiple neoplasms. (Author abstract) (27 Refs)

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2. SCINTIGRAPHY IN EVALUATION OF INTESTINAL ABSORPTION OF FAT DURING RADIOTHERAPY OF CERVIX CANCER.

Modnikov OP
Kirgiz Res. Inst. Oncology and Radiology, Frunze, USSR
Med Radiol (Mosk); 27(2):74-76 1982

The intestinal assimilation and hydrolysis of fat was studied in 97 patients with carcinoma of the uterine cervix. The profile scanning method was used before, during, immediately after and 6-12 mo after telecobalt therapy (total tumor dose 8,000-10,000 rads). Nine patients were in Stage I, 46 in II, 21 in III and 2 in IV. Twenty-seven practically healthy women served as controls. Fat assimilation and hydrolysis were not impaired before radiotherapy compared with controls, but considerable decrease in the rate of resorption and increase in the time necessary for 50% resorption were observed after administration of half the total dose. These changes reached their maxima immediately after administration of the total radiation dose, but there were no significant differences in the impairment of assimilation and hydrolysis. Considerable but incomplete restoration of fat resorption and hydrolysis was observed 6-12 mo after radiotherapy. The improvement in fat hydrolysis was less marked than that in assimilation. (13 Refs) (In RUS)

3. RELIABILITY OF ENDOMETRIAL ASPIRATION CYTOLOGY IN THE ASSESSMENT OF ENDOMETRIAL STATUS.

Morse AR, Ellice RM, Anderson MC, Beard RW
Dept. Cytology, Samaritan Hosp. for Women, Marylebone Road, London NW1 5YE, England
Obstet Gynecol; 59(4):513-518 1982

One hundred twenty women attending routine gynecologic clinics were investigated by endometrial aspiration cytology to determine whether outpatient assessment of endometrial status could be used to determine subsequent patient management. The results show that this technique allows recognition and distinction between cystic hyperplasia, adenomatous hyperplasia, and carcinoma, and the time of the menstrual cycle can be assessed when the endometrium is normal. Endometrial aspiration cytology is valuable in gynecologic practice for determining which women with abnormal bleeding, both premenopausal and postmenopausal, require further investigation. Furthermore, the technique has a role to play in monitoring the status of the endometrium in women at high risk of endometrial malignancy, particularly those receiving hormone replacement therapy. (Author abstract) (22 Refs)

4. CARCINOMA OF THE CERVIX: PERCUTANEOUS LYMPH NODE ASPIRATION BIOPSY.

Edelken-Monroe BS, Zornoza J
(c/o Zornoza) Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
AJR; 138(4):655-657 1982

Percutaneous retroperitoneal lymph node biopsy was performed on 129 patients with carcinoma of the cervix, in whom a lymphangiographic study was reported as suspicious or positive for metastatic nodal disease. Of 159 total biopsies, 114 were performed on external iliac nodes and 45 on paraaortic nodes. An overall accuracy of 68% was obtained without significant complication. The sensitivity of the test was 58% and the specificity 100%. In patients with suspicious lymphangiograms for metastatic disease, percutaneous biopsy identified metastases in 32% of the cases. The predictive value of a negative test was only 42%, but the predictive value of a positive test 100%. (Author abstract) (8 Refs)

5. CLINICAL EXPERIENCE WITH A NEW ENDOMETRIAL CANCER SAMPLING KIT (ISAACS CURITY ENDOMETRIUM CELL SAMPLER) IN THE EARLY DETECTION OF ENDOMETRIAL CANCER.

Feichter GE, Tauber PF, Landowski J
Pathologisches Institut, Universitat Heidelberg, Im Neuenheimer Feld 220-221, D-6900 Heidelberg 1, W. Germany
Acta Cytol (Baltimore); 26(2):141-143 1982

The Isaacs Curity Endometrium Cell Sampler (ICECS) is a new device for the detection of precancerous lesions of the endometrium and asymptomatic endometrial carcinoma. Our clinical experience with the ICECS in a group of 136 women, 45 yr of age and older, with an increased risk for endometrial cancer showed that it was easily used, caused minimal discomfort to the patients and gave good results. The cytologic smears were acceptable for screening in 130 of the 136 cases (95.6%). Normal premenopausal or postmenopausal endometrial cells were found in 100 cases. Hyperplastic changes were found in 18 cases. Carcinomas were diagnosed in 12 cases; all were proven by histologic examination of tissue obtained by curettage. Our results indicate that the new device is valuable for mass cytologic screening for endometrial cancer. (Author abstract) (6 Refs)

6. SCREENING OF ASYMPTOMATIC POSTMENOPAUSAL WOMEN FOR GYNECOLOGIC MALIGNANCIES, WITH SPECIAL REFERENCE TO ENDOMETRIAL SAMPLING METHODS.

Vuopala S, Kauppila A, Mikkonen M, Stenback F
Dept. Obstetrics and Gynecology, Univ. Oulu, SF-90220 Oulu 22, Finland
Arch Gynecol; 231(2):119-127 1981

Three-hundred sixty postmenopausal women given clinical examinations and cytologic smears for gynecologic disease were also screened for endometrial disease by jet wash or pistolet aspiration, and Vabra curettage, and the results compared. Jet wash was successful in 206/360 (57.2%) patients, while pistolet aspiration was possible in 93/154 patients in whom jet wash failed, indicating that pistolet aspiration could have been successful in 299 patients (83.1%), since it uses a smaller cannula than jet wash. Vabra curettage was successful in 274/338 patients, and was not attempted in 22 of the pistolet aspiration failures due to vaginal or cervical stenosis, for a 76.1% rate. Jet wash and pistolet aspiration specimens were inadequate in 3.7% of cases, and Vabra curettage in 44.5%. All studies combined detected 1 mammary and 1 gastric malignancy with ovarian metastases; 4 endometrial and 3 cervical premalignancies; and 52 endometrial or cervical, and 3 mammary benign conditions, for a total detection rate of 15.4%. Pistolet aspiration was thought to be the best method. The use of these methods as screening techniques is discussed. (15 Refs)

7. UTERINE LAVAGE IN THE DIAGNOSIS OF ENDOMETRIAL MALIGNANCY AND ITS PRECURSORS.

Barbaro CA, Fortune DW, Bodey AS, Hennessy E
Dept. Obstetrics and Gynecology, Mercy Maternity Hosp., 126-128 Clarendon St., East Melbourne, Victoria 3002, Australia
Acta Cytol (Baltimore); 26(2):135-140 1982

A negative-pressure uterine lavage technique and simple cytologic processing were employed in the detection of endometrial disease in 1,606 patients, 366 of whom were postmenopausal and asymptomatic. Asymptomatic endometrial cancer and its precursors were detected by lavage in patients with negative cervical smear findings, while some symptomatic patients with negative cervical smears and curettage had persistent lavage cytologic abnormalities that preceded histologic confirmation. This technique detected 90.9% of the adenocarcinomas and 59.1% of the atypical/adenomatous hyperplasia, as compared with 52.3% and 27.3%, respectively, using cervical scraping. Detection rates for endometrial hyperplasia were improved by reporting as abnormal the presence of many clusters of otherwise-normal endometrial cells. In postmenopausal patients, representative endometrial material was obtained in 82.0%, and the procedure was abandoned in 4.1% due to cervical stenosis. Since intrauterine manipulation is unnecessary, the technique was well accepted by elderly asymptomatic women and appears suitable for routine cancer screening. (Author abstract) (17 Refs)

8. CARCINOMA OF THE ENDOMETRIUM: I. A CLINICOPATHOLOGIC STUDY OF CLEAR-CELL CARCINOMA AND SECRETORY CARCINOMA.

Christopherson WM, Alberhasky RC, Connelly PJ
Dept. Pathology, Univ. Louisville Sch. Medicine, Health Sciences Center, Louisville, KY, 40292
Cancer; 49(8):1511-1523 1982

In a pathologic review of 1,224 cases of endometrial carcinoma, 1,023 were confirmed cases of endometrial carcinoma. Fifty-six (5.5%) were clear-cell adenocarcinoma (CCE). Fifteen cases of 'secretory carcinoma' (SCE) were examined for comparison. Fifty-five patients with CCE and all with SCE were followed for at least 5 yr or until death. There were only 19 survivors among those with CCE. No 5-yr survivor subsequently died of disease. Of the 15 patients with SCE, 13 survived for 5 yr although two additional patients died of recurrent disease at 5.4 and 7 yr. All survivors of CCE were Stage I patients at the time of diagnosis. All were postmenopausal, and had a median age of 67 yr compared with 58 yr for patients with SCE. Unlike SCE, the morphology of CCE was preserved in the subsequent hysterectomy specimen, in the recurrent disease, and in the metastases. CCE was proportionately more common in black women and the 5-yr survival was only 12.5% as compared with 39.1% for white women. In contrast to endometrial carcinoma in general, most women who failed treatment died of disease. There was no increase in the relative frequency over the 23-yr time period of the study. Age at time of diagnosis seemed to be an important prognosticator. Prognosis also correlated well with stage of disease and depth of myometrial invasion. It correlated to a somewhat lesser extent with the method of treatment and had a poor correlation with the histologic pattern or degree of cellular differentiation: however, essentially all tumors were considered to be poorly differentiated. Finally, a histologic tissue marker in the form of hyalin-like, PAS-positive, diastase-resistant bodies was found in the 64% of the women with CCE. (Author abstract) (34 Refs)

9. CYTOLOGICAL STUDIES ON EARLY INVADING PATTERNS IN UTERINE CERVICAL CANCER.

Miyazaki Y, Iwasaki M, Tojo S, Hasegawa K
Dept. Obstetrics and Gynecology, Kobe Univ. Sch. Medicine, Kobe, Japan
Nippon Gan Chiryo Gakkai Shi; 16(7):1397-1407 1981

Based on examination of 347 cases of early-stage uterine cervical cancer, 30 of intraepithelial cervical cancer, and 30 of invasive cervical cancer, early-invading patterns of uterine cervical cancer were classified into the following six types: migrating (M), probing finger (PF), epithelial bud (EB), nodular growth (NG), epithelial cord (EC), and embolic spread (ES). Relationships between the pathohistological patterns and cytological findings for the surgical specimens were studied. Frequencies of malignant cells among the abnormal cells observed in the M-, PF-, and EB-type cytological smear specimens were similar to those observed in carcinoma in situ specimens; frequencies of malignant cells in the NG-, EC-, and ES-type specimens were similar to those observed in the invasive cervical cancers. Malignant cells were classified according to the system of Graham, Koss, Tweeddale, and Dubilier. Based on this system, the frequencies of particular types of malignant cells in M-, PF-, and EB-type specimens were not too different from those in carcinoma in situ; marked differences in the frequencies of particular types of malignant cells were observed between the NG-, NC-, and ES-type specimens and carcinoma in situ. With respect to cellular arrangement, nuclear chromatin pattern, and frequency of nucleoli in the malignant cells, M- and PF-type specimens were similar to carcinoma in situ, and EC- and ES-type specimens were similar to invasive cancer. Cytological studies can give information enabling differential diagnosis of early-invading cancer from carcinoma in situ and from invasive cancer and allowing the typing of specimens of early-invading uterine cervical cancer. (36 Refs) (In JPN)

10. ADENOID CYSTIC CARCINOMA OF THE UTERINE CERVIX: ULTRASTRUCTURE, IMMUNOFLUORESCENCE, AND CRITERIA FOR DIAGNOSIS.

Mazur MT, Battifora HA
Dept. Pathology, Jewish Hosp. St. Louis, P.O. Box 14109, 216 South Kingshighway, St. Louis, MO, 63178
Am J Clin Pathol; 77(4):494-500 1982

An example of adenoid cystic carcinoma of the cervix was recently encountered in our laboratory and studied by histochemistry, electron microscopy, and immunofluorescence in order to compare the neoplasm with adenoid cystic tumors at other sites and to establish criteria for diagnosis. Histochemically, cervical adenoid cystic carcinoma showed the two types of mucin, epithelial and stromal, as expected in adenoid cystic carcinomas of other organs. Ultrastructurally, this tumor was characterized by redundant basal lamina forming pseudocysts, intercellular spaces, and occasional true lumens with microvilli. Immunofluorescence studies showed that the cells contain at least two antigenically different types of filaments, actin and keratin, and that the cells produce true basement membrane (collagen IV). The presence of actin suggests myoepithelial differentiation even though the tumor probably originated from the cervical reserve cells, and myoepithelium is not a known component of normal cervix. This study shows that cervical adenoid cystic carcinoma is a distinct entity which can be identified and separated from other types of cervical adenocarcinomas. (Author abstract) (19 Refs)

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11. HISTOLOGICAL CRITERIA FOR THE PROGNOSIS IN PATIENTS WITH OPERATED SQUAMOUS CELL CARCINOMA OF THE CERVIX.

Baltzer J, Lohe KJ, Kopcke W, Zander J
I. Frauenklinik der Universitat Munchen, Maistrasse 11, 8000 Munich 2, W. Germany
Gynecol Oncol; 13(2):184-194 1982

Histological criteria for the prognosis were examined in 718 surgical specimens with squamous cell carcinoma of the cervix which were subjected to uniform histological workup. In the distinction between the invasion front and the tumor center the tumor grading in the region of the invasion front had particular prognostic significance. A very pronounced dissociative tumor growth also had an influence on the 5-yr survival rates. The poorest prognosis was registered with patients in whom an invasion of the carcinoma into blood vessels could be observed. Taking into account the inflammatory stroma reaction in the center of the tumor and at the invasion front, more favorable recovery results could be registered with a heavy inflammatory infiltration in the region of the invasion front. The increase in tumor volume lead to a deterioration of the recovery rates. These poorer recovery rates were due to the increase of the macrometastases, whereas tumor cell embolization into lymph nodes did not significantly influence the recovery results. (Author abstract) (48 Refs)

12. TWO TYPES OF CELLS IN THE NORMAL AND ATYPICAL SQUAMOUS EPITHELIUM OF THE CERVIX. II. LIGHT MICROSCOPIC STUDY IN HUMAN SUBJECTS.

Rubio CA
Dept. Pathology, Karolinska Sjukhuset, S-104 01 Stockholm 60, Sweden
Acta Cytol (Baltimore); 26(2):121-125 1982

The occurrence of two morphologically distinct cell types in the human cervical epithelium is reported. One of the two cell types had a large nucleus with scant chromatin, two to three chromocenters and thin chromatinic membrane. Cells with these characteristics were called cells with 'lucid nuclei.' The other cell type had a small, dark nucleus. These types of cells were present in film-coated autoradiograms of specimens that had been fixed in Carnoy's solution; they were readily observed by altering the quality of the light illuminating the preparations. Micrometric determinations confirmed that cells with 'lucid nuclei' were larger than cells with 'nonlucid nuclei.' There was significant variation in the proportion of cells with 'lucid nuclei' among the various individuals investigated; these variations were not age dependent. Individual variations in the proportion of cells with lucid nuclei were also observed among cervical dysplasias and carcinoma in situ. (Author abstract) (6 Refs)

13. CARCINOEMBRYONIC ANTIGEN SERUM LEVELS IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX: CLINICAL SIGNIFICANCE.

te Velde ER, Persijn JP, Ballieux RE, Faber J
Dept. Gynecology, Univ. Hosp., Catharijnesingel 101, 3500 CG Utrecht, The Netherlands
Cancer; 49(9):1866-1873 1982

In 114 patients with invasive cervical cancer of the squamous cell type pretreatment CEA levels were determined. An individual upper limit of the normal range was derived taking into account the smoking habits and the age of each patient. Pretreatment CEA levels exceeding the upper limit of normal concurred with a very poor prognosis, regardless of the stage of the tumor. Moreover, in 92 patients longitudinal CEA patterns were established. The median follow-up time of the non-recurrence patients was 4 yr. Three patterns appeared to be exclusively associated with the presence of recurrent cancer. The median lead-time obtained in patients demonstrating such patterns, was 13 wk. The clinical value and the possible therapeutic consequences of the findings presented are discussed in relation to the available knowledge of tumor growth in cervical cancer. (Author abstract) (39 Refs)

14. CYTOPHOTOMETRIC DETERMINATIONS OF DNA, HISTONE, ARGININE, LYSINE, AND THEIR CONCENTRATIONS IN EU- AND HETEROCHROMATIN OF THE CELL NUCLEUS OF DYSPLASIAS, CARCINOMA IN SITU, AND CARCINOMA OF THE HUMAN CERVIX UTERI.

Herzog RE
Universitats-Frauenklinik, Langenbeckstrasse 1, D-6500 Mainz, W. Germany
Arch Gynecol; 231(2):91-98 1981

The amount of DNA, histone, arginine, and lysine was determined by cytophotometry, planimetry, and selective photometry in cell nuclei from fixed cervical smears from controls, and patients with mild cervical dysplasia (8), moderate dysplasia (9), severe dysplasia (11), carcinoma in situ (19), and invasive carcinoma (24). In addition, differences between euchromatic and heterochromatic areas of the nuclei were measured. Experimental cells had higher levels of DNA, histone, arginine, lysine, heterochromatin, hetero-histone, hetero-arginine, and hetero-lysine than controls. In all cases the hetero-structures had higher values than the eu-structures, and these were in the same range for the patient groups. Differences in DNA and arginine levels were similar, in histones were significantly greater (p less than 0.05) for moderate dysplasia and carcinoma in situ, and for lysine were significantly higher (p less than 0.01) in hetero-structures. Relationships were not changed significantly by carcinogenesis. (48 Refs)

15. CHROMOSOMIC CHANGES IN 20 LESIONS OF CERVIX UTERI.

Kiricuta I, Suciu St, Giurgiuman M
(c/o. Suciu) Institutul Oncologic, Strada Republicii 34 - 36, R - 3400 Cluj-Napoca, Romania
Arch Geschwulstforsch; 52(3):205-211 1982

Twenty patients (28-60 yr old) had uterine cervical dysplasia (CD: 5) carcinoma in situ (CAS: 2), and invasive cancer (ICA Stage I to Stage III: 13 patients). Biopsies of lesions were removed before any treatment, processed, slides prepared, stained, and examined. Number of chromosomes (NC) in 4/5 CD were in peridiploid region, while in 1/5 they ranged from hypodiploidy to hypertriploidy; in CAS the NC varied from 41-82; in 2/13 ICA were peridiploid, 1/13 was hyperdiploid to hypertetraploid, and 10/13 ranged from triploid to hypertetraploid. Chromsome 1 was abnormal in 1/5 CD and 10/13 ICA. Long acrocentric was present in 1/5 CD and in 3/13 ICA. Medium size metacentric was observed in 3/13 ICA. Other markers observed consisted of minute chromosomes in 2/13 ICA, and double minute bodies in 1/13 ICA. Variety in chromosomic changes is characteristic of uterine cervical lesions, while in others one characteristic abnormality is present. Acrocentric marker is a general indicator of malignant growth. Complete or partial trisomy of long arm of chromosome 1 is found in cancers of breast, cervix, lung, ovary, melanoma, and

others. Abnormalities in chromosome 1 usually indicate advanced cancer. (22 Refs) (In GER)

16. CHARACTERIZATION OF TUMOR-ASSOCIATED ANTIGEN FROM HUMAN CARCINOMA OF THE UTERINE CERVIX.

Nadkarni JJ, Satam MN, Damle SR, Rajpal RM, Nadkarni JS
Immunology Div., Cancer Res. Inst., Parel, Bombay 400012, India
Gynecol Oncol; 13(2):175-183 1982

In vitro demonstration of cell-mediated immune responses to tumor-associated antigen (TAA) was observed with autologous tumor extracts from patients with cervical cancer. Seventy-six percent of these patients exhibited an inhibitory effect with autologous antigens while 59% reacted with homologous antigens. A progressive rise in percentage inhibitory activity was associated with increasing stage of the disease. The physicochemical and immunochemical characterization of the TAA found on the membrane of cervical tumor cells suggested that it may be a lipid-protein complex containing an enzyme having immunological determinants such as those of term-placental alkaline phosphatase enzyme. (Author abstract) (24 Refs)

17. ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY TO HERPES SIMPLEX VIRUS-TRANSFORMED CELLS IN THE COURSE OF CERVICAL CARCINOMA.

Christenson B
Dept. Epidemiology, Natl. Bacteriological Lab., S-105 21 Stockholm, Sweden
Am J Epidemiol; 115(4):556-568 1982

The antibody-dependent cell-mediated cytotoxicity assay was used to determine whether humoral antibodies from women with cervical carcinoma in the presence of normal mononuclear cells could induce cytotoxicity to hamster embryo fibroblasts, originally transformed by herpes simplex virus Type 2 (HSV-2) (333-8-9), to a cervical carcinoma cell line (ME-180) and to a lung carcinoma cell line (A-549). Control groups consisted of 81 age-matched healthy women and 77 patients suffering from malignancies other than cervical carcinoma. Significant cytotoxicity to HSV-2-transformed cells was observed in sera from 20 of 28 (71%) surviving patients with cervical cancer who were followed with serum samples collected 6-24 mo after initial treatment. Comparison of serum samples obtained before initial treatment from 20 patients surviving the observation period of 60 mo or longer and from 20 patients who died during the observation period showed that the survivors had significantly higher cytolytic activity prior to treatment. Long-term survivors also showed a drop in cytolytic activity in sera obtained 30 mo or later after treatment. Patients with long survival but whose cancer finally caused death, had stronger cytolytic activity than those with short survival (24 mo or less). Patients with cervical cancer had significantly higher cytolytic activity to HSV-2-transformed cells and to the cervical carcinoma cells (ME-180) than age-matched control women and patients with malignancies other than cervical carcinoma. (Author abstract) (33 Refs)

18. PARADOXICAL HYPERSECRETION OF GROWTH HORMONE IN PATIENTS WITH ENDOMETRIAL ATYPICAL HYPERPLASIA AND CARCINOMA: EFFECT OF HYSTERECTOMY.

Ayalon D, Peyser MR, Limor R, Lessing JB, Ravid R
Inst. Reproductive Endocrinology, Dept. Obstetrics and Gynecology A, Municipal Governmental Medical Center, Univ. Tel Aviv, Tel Aviv, Israel
Gynecol Obstet Invest; 13(1):9-16 1982

Serum human growth hormone (HGH) levels and HGH responses to fasting glucose tolerance tests (GTT) were studied in 3 groups of age-matched postmenopausal women (53-65 yr old): 8 women scheduled for radical hysterectomy (hstx) for endometrial carcinoma (3/8) or atypical hyperplasia (5/8); 8 women scheduled for other gynecologic surgery for non-endometrial diseases; and 8 healthy women. None of the women was obese or diabetic. Baseline fasting glucose and HGH levels were normal in all groups. Urinary estrogen levels were within the normal postmenopausal range. The patients with endometrial neoplasms showed paradoxical HGH hypersecretion in response to GTT. When a repeat GTT was performed 6 mo after hstx, the paradoxical HGH reaction was absent. Since the controls awaiting surgery for non-endometrial diseases did not show a paradoxical HGH reaction to GTT, fasting and preoperative anxiety seemed to be ruled out as being responsible for the disturbance of HGH secretion in the patients with endometrial hyperplasia or cancer. The results suggested that the abnormal HGH responses might have been caused by some HGH-releasing factor in the malignant and premalignant endometrial tissues. (21 Refs)

19. OESTROGEN PRODUCTION IN ADIPOSE TISSUE FROM NORMAL WOMEN AND WOMEN WITH ENDOMETRIAL CANCER IN VITRO.

Folkerd EJ, Reed MJ, James VH
Dept. Chemical Pathology, St. Mary's Hosp. Medical Sch., London W2 1PG, England
J Steroid Biochem; 16(2):297-302 1982

The conversion of androstenedione (AND) to estrone (ES), and ES to estradiol (ESL) in human adipose tissue obtained from women of various ages and body wt and from those with endometrial cancer was investigated. Subcutaneous adipose tissue was obtained from the abdominal wall of women undergoing gynecological surgery. The conversion of AND to EST in adipose tissue was not correlated with the percentage excess wt of the women. The mean conversion of AND to EST for women 40-50 yr old was 19.6 picog EST/mg protein/3 hr, compared with 3.2 picog EST/mg protein/3 hr in women between 20 and 39 yr. Postmenopausal women had conversion rates less than 11 picog/mg protein/3 hr, indicating that the efficiency of aromatization may decline in later years. The mean conversion of EST to ESL in women 40-50 yr old was 5.1 nanog/mg protein/hr, compared with 1.3 nanog/mg protein/hr for women 20-39 yr old. No increase in rate of conversion of AND to EST in sc adipose tissue was observed in women with endometrial cancer compared with normal women of similar age and wt. In one woman with endometrial cancer, a high rate of conversion of AND to EST (104 picog/mg protein/3 hr) was observed, while the conversion of EST to ESL was lower (1.3 nanog/mg protein/hr), indicating that steroid metabolism is not uniform in adipose tissue throughout the whole body. Thus, adipose tissue can aromatize AND to EST and reduce EST to ESL in vitro. (22 Refs)

20. IN VIVO AVAILABILITY OF CIRCULATING ESTRADIOL IN POSTMENOPAUSAL WOMEN WITH AND WITHOUT ENDOMETRIAL CANCER.

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Obstet Gynecol; 59(4):416-421 1982

To assess the in vivo effect of plasma proteins on the tissue availability of circulating estradiol in postmenopausal women with endometrial cancer, the transport of tritiated estradiol across the brain capillary wall, ie, the blood-brain barrier, was examined in anesthetized rats using a tissue sampling-single injection technique. Serum samples were studied from 25 women with endometrial cancer and from an equal number of women without the disease who were matched to the cancer patients for age and percent ideal wt. The mean +- SE brain uptake indices of estradiol, using serum from the cancer patients and controls, were 40.7 +-2.8 and 33.9 +-2.6, respectively. This difference was not statistically significant. Positive correlations were observed between the brain uptake index and percent ideal wt in the cancer ($r = 0.65$) and in the control ($r = 0.21$) subjects. Linear regressions of the reciprocal of the brain uptake index and levels of sex hormone-binding globulin showed strong correlations ($r = 0.78$) in both groups of patients, whereas correlation coefficients between the brain uptake index and percentage sex hormone-binding globulin were $r = 0.86$ and $r = 0.98$ for the cancer and the control subjects, respectively. These latter observations support the concept that the brain uptake index reflects the effects of plasma proteins on transport of estradiol across a capillary wall. The findings of this study indicated that (1) the fraction of estradiol available for transport across the blood-brain barrier greatly exceeded the free (dialyzable) moiety and was essentially equal to the albumin-bound and free (dialyzable) fractions of the plasma hormone; and (2) the tissue availability of estradiol was influenced by the body size of the subjects, particularly in the cancer patients, with more circulating estradiol being available in the obese women. This observation suggests that obese, older women are at dual risk of the action of estradiol at the tissue level. They have higher total levels and proportionately greater bioavailable fractions than slender subjects. (Author abstract) (24 Refs)

21. THE EARLY POSTOPERATIVE AS WELL AS THE LATE CONSEQUENCES OF CERVIX CONIZATION. A CRITICAL EXAMINATION OF 414 CONIZATIONS.

Moinian M, Andersch B
Kvinnokliniken, Ostra Sjukhuset, S-416 85 Goteborg, Sweden
Geburtshilfe Frauenheilkd; 42(2):123-126 1982

In a series of 414 patients with cancer in situ cervicis uteri and cervix conization, retrospectively are the incidence of early postoperative complications and the late consequences of this operation during a follow-up time of 5 to 10 yr studied. Postoperative bleeding occurred in 92 cases (22%). Over half, 52 patients, had their hemorrhage within 6 hr after the operation. In 6% of postoperative bleedings suture of cervical wound was necessary, when the rest could be controlled only by conservative measurements. The late consequences of cervix conization were numerous and serious. 4.8% of women with cervix conization in future developed a cervix stenosis, which repeatedly required cervix dilatation under general anesthesia. Moreover, 5.5% of the conized patients had later to suffer from a severe dysmenorrhea. In a total of 923 pregnancies the risk of obstetrical complications before and after cervix conization was analyzed. 20.5% of all pregnancies following cone biopsy were complicated by a cervix factor, cervix incompetency or cervical dystocia. After conization there was seven times higher incidence of late spontaneous abortion than before. (Author abstract) (47 Refs) (In GER)

22. ASSESSMENT OF FAILURES OF CRYOSURGICAL TREATMENT IN CERVICAL INTRAEPITHELIAL NEOPLASIA.

Stuart GC, Anderson RJ, Corlett BM, Maruncic MA
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Am J Obstet Gynecol; 142(6,part1):658-663 1982

The overall recurrence rate in 166 patients treated with cryosurgery is 10.8%. Recurrent cervical intraepithelial neoplasia is much more common in patients with severe dysplasia. Failures are commonly due to one of four factors. First, cryosurgery is to be used only after adequate colposcopic assessment and a negative endocervical curettage. Cryosurgery is a safe, effective treatment in selected patients, but consideration of surgical management should be given in the older patient who has completed childbearing, particularly those with severe dysplasia or carcinoma in situ. A full 7-min freeze with optimum application of the cryoprobe to the full affected surface is essential. Careful follow-up of these patients is mandatory The majority of failures occur within the first 12 mo and probably represent persistent rather than recurrent disease. (Author abstract) (17 Refs)

23. VOIDING DISORDERS AFTER RADICAL HYSTERECTOMY.

Carenza L, Nobili F, Giacobini S
Dept. Obstetrics and Gynecology, Univ. Rome, Rome, Italy
Gynecol Oncol; 13(2):213-219 1982

The authors report the reaction on bladder function observed in 15 women suffering from cervical cancer in Stages I and II after the Wertheim-Meigs radical hysterectomy. All the patients were given various tests before and after operation: urodynamic investigations using uroflowmetry, gas cytometry completed by a urecholine denervation test, cystosphinctermanometry with simultaneous flowmetry, simultaneous recording of bladder and urethral pressures with flowmetry, and urethral closure pressure profile with microtip transducers (Millar Instruments). On the basis of the results, the authors maintain that the damage caused by the operation affects not only the detrusor but also the normal sphincter function as suggested, in fact, by the symptoms observed in the patients (dysuria and stress incontinence). the preoperative urodynamic study was of no help in foreseeing the amount of damage caused by the operation to the normal bladder-sphincter function. On the other hand, the study proved essential postoperatively in clarifying the pathophysiology of the voiding disorders complained of by the patients and, above all, in deciding upon the best plan of management. (Author abstract) (6 Refs)

24. RECURRENT CANCER OF THE CERVIX FOLLOWING RADICAL HYSTERECTOMY AND PELVIC NODE DISSECTION.

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Dept. Obstetrics and Gynecology, Medical Coll. Virginia, Virginia Commonwealth Univ., MCV Station, Richmond, VA, 23298

Obstet Gynecol; 59(4):422-427 1982

Forty patients with recurrence following radical surgery for early invasive cancer of the cervix were studied. Fifty-eight percent of the recurrences were observed within the first 12 mo after surgery and 83% within the first 2 yr. The site of recurrence was found to influence diagnosis, symptomatology, clinical findings, prognosis, cause of death, and therapy. The prognosis for patients with recurrent cervical cancer was poor, with only five patients (13%) surviving free of disease after 5 yr. One patient is presently alive and without disease for more than 2 yr. Patients who did not receive a potentially curative course of radiation therapy at the time of diagnosis of the recurrence had a poor prognosis. None of the patients managed by exenterative procedures or chemotherapy survived. Guidelines are suggested for follow-up after primary radical hysterectomy and pelvic node dissection. (Author abstract) (11 Refs)

25. STUDY OF G2-M STAGE SYNCHRONIZATION OF UTERINE CERVICAL CARCINOMA CELLS DUE TO RADIATION THERAPY, WITH EMPHASIS ON MEASUREMENT AND CLINICAL SIGNIFICANCE QUANTITY OF DNA.

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Dept. Obstetrics and Gynecology, Jikei Univ. Sch. Medicine, Tokyo, Japan

Nippon Gan Chiryo Gakkai Shi; 16(7):1456-1467 1981

Changes in cellular DNA due to irradiation were studied in 20 patients with uterine cervical cancer and in nude mice bearing human uterine cervical carcinoma. The DNA was measured with the aid of microspectrophotometry in Feulgen-stained human carcinoma cells from biopsy specimens of all 20 patients when they had received 500 rad of irradiation, 18 of the patients when they had received 1,000 rad, and 15 of the patients when they had received 2,000 rad. The av quantity of nuclear DNA (units not defined) in the cells increased with the quantity of radiation received (1.31 for 500 rad, 1.45 for 1,000 rad, and 1.87 for 2,000 rad). Av diameter of the nuclear DNA also increased with quantity of radiation received and was related to the increase in the av quantity of nuclear DNA. Similar tendencies were observed in the cervical cancer cells transplanted in the mice. Flow-microfluorometric analysis of the DNA of the transplanted cells indicated that the irradiation induced change in repopulation and redistribution of cycling cells and partial synchronization of the cells to the G2-M stage. Five-yr observation of the patients given 500 rad irradiation indicated that good prognosis (12/20 patients) was associated with increased quantity (10/12) and diameter (9/12) of the cellular DNA. High frequency of G1 stage residual cells in the cancer patients who received 2,000 rad irradiation was associated with poor prognosis, since the G1 stage cells survived a long time and were not very radiosensitive. (36 Refs) (In JPN)

26. TAMOXIFEN AND AMINOGLUTETHIMIDE IN THE MANAGEMENT OF PATIENTS WITH ADVANCED ENDOMETRIAL CARCINOMA NOT RESPONSIVE TO MEDROXYPROGESTERONE.

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Dept. Obstetrics and Gynaecology, Univ. Melbourne, Melbourne, Australia

Aust NZ J Obstet Gynaecol; 21(4):226-229 1981

Eleven (58-74-yr old) females with recurred endometrial adenocarcinoma were treated for 8 wk with tamoxifen (T: 20 mg/d, bid) or aminoglutethimide (AG: 250 mg/d, bid; 250 mg/d increase every 2 days) until adrenal blockade effected reduction of plasma dehydroepiandrosterone sulfate to at least 50% of base line value. Cortisone acetate and fluorocortisone were used as replacement therapy. The second drug was added after the 8 week evaluation only when response was progression, regardless of T or AG being first. A partial or complete initial response resulted in indefinite continuation of initial therapy with monthly review, or until progression resumed. Toxic effects included nausea from T sufficient to change treatment to AG in two subjects, lethargy common from AG, and intermittent dizziness in two subjects from AG. Details of six cases are presented. Both drugs are indicated to be useful in subjects resistant to medroxyprogesterone. (37 Refs)

27. RADICAL PELVIC SURGERY VERSUS RADICAL SURGERY PLUS RADIOTHERAPY FOR STAGE IB CARCINOMA OF THE CERVIX UTERI. PRELIMINARY RESULTS OF A PROSPECTIVE RANDOMIZED CLINICAL STUDY.

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Arch Geschwulstforsch; 52(3):223-229 1982

Results of a follow-up from 1976-1979 of 120 patients with carcinoma of the cervix uteri are presented. Sixty patients were treated with radical surgery alone and 60 with surgery plus radiotherapy [52 Gray Units (Gy) tumor dose to the whole pelvis by external radiation; 2 Gy/day beginning 6 wk after surgery]. All carcinomas were subdivided by histological grading into highly differentiated, moderately differentiated, and undifferentiated tumors. During the first yr all patients were examined at 2-mo intervals, and then every 3 mo up to the end of yr 3, and at 6-mo intervals thereafter. The av follow-up period was 44 mo (24-72 mo). No significant differences between the groups were observed with regard to prognostic factors. Comparing the different therapeutic regimens up to 18 mo, significantly better results were observed for patients treated with surgery alone. After that period no significant differences were observed. In patients treated with surgery alone, three central or parametrial recurrences were diagnosed. Three patients treated by combined therapy developed distant metastasis. Only minor complications caused by therapy were observed: strictures of the bowel (3), hydronephroses (3), and lymphedemas (17). Leg edemas were more frequent in patients treated by combined therapy than in those treated by surgery only. (35 Refs)

28. LYMPH NODE METASTASES FROM CARCINOMA OF THE CERVIX, STAGES IB AND IIA: IMPLICATIONS FOR PROGNOSIS AND TREATMENT.

Fuller AF, Elliott N, Kosloff C, Lewis JL
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Gynecol Oncol; 13(2):165-174 1982

The significance of lymph node metastases (LNM) for prognosis and treatment of cervical carcinoma was studied in 431 patients who underwent radical hysterectomy for Stage IB or IIA disease. Lymph node dissection was performed on 418 patients, of whom 71 had LNM. Incidence of LNM was 15% of 42 patients with Stage IB and 22% of 29 patients with Stage IIA disease. Unilateral LNM were found in 52 patients and bilateral LNM in 19 patients. Forty-one patients had only one LNM; 14/71 had three or more LNM. Thirty-two patients with pelvic LNM received postoperative radiotherapy (mean dose 4,000 rad over 4 wk); 39 patients received no further treatment. After a mean 90 mo, 36 patients were alive and free of disease. Twenty-seven had died of recurrent tumor, 1 was alive with recurrent tumor, 4 died of complications, and 3 were lost to follow-up. Median time between surgery and recurrence was 10 mo; median survival time after detection of recurrence was 6 mo. Factors predictive of recurrence included the number of LNM, tumor histology, tumor extension beyond the cervix, menopausal status, and size and extension of the primary cervical tumor. Tumors recurred in 32% of patients with one or two LNM and 71% of patients with three or more LNM. No advantage was demonstrated for postoperative radiotherapy. Cure was achieved in 10/56 patients without LNM who had recurrent tumor; none of the patients with LNM who developed recurrent tumor were cured. (14 Refs)

29. CLINICAL SIGNIFICANCE OF UTERINE BODY INVASION IN UTERINE CERVICAL CANCER.

Noguchi H, Tsukahara Y, Shiozawa K, Tsukamoto T, Shiozawa I, Sakai Y, Fukuta T, Iwai S
Dept. Obstetrics and Gynecology, Shinshu Univ. Faculty Medicine, Matsumoto-shi, Nagano Prefecture 390, Japan
Nippon Gan Chiryo Gakkai Shi; 16(7):1358-1364 1981

Presence or absence of invasion of the uterine body by uterine cervical cancer was investigated in 289 cases of cancer of the uterine cervix. All 289 cases were treated with radical complete hysterectomy. Invasion of the uterine body was observed in 64/289 cases; the invasion involved the endometrium in 13/64, muscle layers in 43/64, and serosal layers in 8/64. Invasion of the uterine corpus occurred in 10/139 Stage I uterine cervical cancer cases, 52/146 Stage II, and 2/4 Stage III. Cases that had invasion of the uterine body also had high frequency of metastasis to the vaginal wall, perimetrium, and lymph nodes. According to the CPL classification system, the frequency of uterine body invasion was highest in the Type L cases. Five-yr survival rate of the patients who had cancerous invasion of the uterine body was 25/51; this was low compared to that (161/181) for those without invasion. Intraabdominal or lymph node metastases were frequent in 23 patients who had recurrence; 19/23 patients had recurrence within 3 yr of surgery. The results suggested that the possible presence of cancerous invasion of the uterine body must be considered when treating uterine cervical cancer. (9 Refs) (In JPN)

30. PULMONARY METASTASIS OF CARCINOMA OF THE CERVIX: A RETROSPECTIVE STUDY.

Tellis CJ, Beechler CR
Walter Reed Army Medical Center, Washington, DC, 20012
Cancer; 49(8):1705-1709 1982

The medical records of 243 patients admitted over a 5-yr period with a diagnosis of carcinoma of the cervix were reviewed to determine (1) the frequency of pulmonary metastasis, (2) the relationship between the stage of the primary lesion and the incidence of pulmonary metastasis, and (3) the relationship between the disease-free interval and the incidence of pulmonary metastasis. We found that pulmonary metastasis had developed in 22 of 243 patients. Pulmonary metastasis occurred in 4.24% of all patients with Stage I carcinoma of the cervix; in 13% of all patients with Stage II; 7.4% of all patients with Stage III; and 57% of all patients with Stage IV disease. The av disease-free interval was 39 mo in Stage I disease; 37.3 mo in Stage II disease; 18 mo in Stage III disease; and less than 1 mo in Stage IV disease. The most common roentgenographic pattern was that of multiple pulmonary nodules (13 of 22 patients). Twenty five percent (5 of 20) of patients with pulmonary metastasis had no evidence of other metastasis. (Author abstract) (13 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

31. THE PATHOLOGICAL ASSESSMENT OF OVARIAN NEOPLASMS V: THE GERM CELL TUMORS.

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Pathology; 14(1):47-72 1982

All neoplasms of the ovary encountered in a 25-yr study period at King George V Memorial Hospital were classified according to the World Health Organization (WHO) Histological Classification of Ovarian Tumors. Of just fewer than 1,700 tumors, 467 fell into the category designated as germ cell tumors: 4 dysgerminomas, 1 endodermal sinus tumor, 1 primary choriocarcinoma, 6 immature and 454 mature teratomas and 1 mixed malignant germ cell tumor. Two additional cases of gonadoblastoma with associated dysgerminoma were encountered and included for discussion. A detailed histological assessment is presented and the major clinical correlates are documented. (Author abstract) (81 Refs)

32. A STUDY OF AUTOPSIED CASES OF LYMPHOGENOUS DISSEMINATION OF OVARIAN CANCER.

Iurkova LE, Vinokurov VL
N. N. Petrov Res. Inst. Oncology, USSR Ministry Health, Leningrad, USSR
Vopr Onkol; 28(1):34-38 1982

A clinicopathological study of 152 autopsied cases of ovarian cancer was carried out. Metastases in lymph nodes ranked third (57.9%), following lesions in the peritoneum (92.1%) and greater omentum (79.6%). metastases in lymph nodes were found in 88 cases; almost invariably, they were concomitant with implantation and hematogenous metastases. The sites of lymphogenous lesions were most frequently in paraaortal (72.7%), pelvic (47.7%) and mesenteric (27.3%) lymph nodes. No metastases in lymph collectors were detected in nearly half

the cases (42.1%) of generalized malignancy. It was shown that lymphogenous dissemination does not necessarily predominate in the clinical picture even at the terminal stage of the disease. (Author abstract) (10 Refs) (In RUS)

33. POLYEMBRYOMA OF OVARY PRODUCING ALPHA-FETOPROTEIN AND HCG: IMMUNOPEROXIDASE AND ELECTRON MICROSCOPIC STUDY.

Takeda A, Ishizuka T, Goto T, Goto S, Ohta M, Tomoda Y, Hoshino M
Lab. Ultrastructure Res., Aichi Cancer Center Res. Inst., Chikusaku, Nagoya 464, Japan
Cancer; 49(9):1878-1889 1982

Polyembryoma of ovary producing alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) was studied by indirect immunoperoxidase method for AFP and HCG, and electron microscopy. Clinically, this patient showed pseudoprecocious puberty caused by elevated HCG which is synthesized by trophoblastic cells in polyembryoma. She is put under VAC (vincristine, actinomycin-D, cyclophosphamide) chemotherapy after operation and shows no signs of recurrence including reelevation of serum AFP at 5 mo after operation. Embryoid bodies which we studied correspond to normal embryo at 15- or 16-day stage. Immunoperoxidase study showed that AFP is synthesized by yolk sac cells of the embryoid bodies and HCG is synthesized by syncytiotrophoblastic cells. The finding about AFP synthesis suggests that normal embryo at 15-or 16-day stage may begin AFP synthesis. Electron microscopic study showed that each part of the embryoid bodies had some characteristic structures. Most striking features found in the cytodifferentiation of the embryoid bodies were noticed in some special differentiation of plasma membrane and existence of surface coat. Desmosomes were found in endodermal cells and yolk sac cells. Ectodermal cells were attached to each other by zonulae occludentes and adherentes. Microvilli were found in ectodermal cells and yolk sac cells. Two different kinds of surface coat were found in mesodermal cells and lining cells of yolk sac cavity: thin-layered deposit of electron-dense material covering the plasma membrane facing intercellular space of mesodermal cells and endodermal cells, and thick-layered deposit of electron-dense material which covered the plasma membrane facing yolk sac cavity of endodermal cells and yolk sac cells. Presence of similar characteristic material in RER of yolk sac cells led us to speculate that thick deposit was synthesized by yolk sac cells and secreted into yolk sac cavity. Combined with immunoperoxidase study by light microscopy, we assume that this thick-layered deposit has some close relation to AFP. (Author abstract) (23 Refs)

34. DIAGNOSTIC SIGNIFICANCE OF PREGNANCY-ASSOCIATED ALPHA2-GLYCOPROTEIN IN PATIENTS WITH OVARIAN CANCER.

Sawada M, Shimizu Y, Okudaira Y, Matsui Y, Nishiura H, Hayakawa F.
Div. Gynecology, Dept. Clinical Res., Res. Inst. Microbial Diseases, Osaka Univ., Yamada-kami, Suita-City, Osaka, Japan
Gynecol Oncol; 13(2):229-236 1982

Pregnancy-associated alpha2-glycoprotein (alpha2-PAG) levels were measured in several kinds of samples by a modification of Laurell's electroimmunoassay using a rabbit anti-alpha2-PAG serum. Samples were sera obtained from healthy females (46 cases), patients with benign ovarian tumors (8 cases), patients with ovarian cancers (18 cases), nude mice bearing heterotransplanted human ovarian cancers (4 cases), and ascites and urine of cancer patients. Serum alpha2-PAG levels in patients with benign ovarian tumors were 3.8 +-3.2 U/ul and almost the same as those of controls (2.6 +-3.0 U/ul). However, serum alpha2-PAG levels were higher in patients with ovarian cancers (12.0 +-3.7 U/ul). alpha2-PAG was scarcely detected in ascites or urine obtained from cancer patients, and was not detected in sera of tumor-bearing nude mice, despite the high levels of alpha2-PAG in those of original patients. The reliability of alpha2-PAG as a tumor-associated marker in patients with ovarian cancer was reinforced by the comparison of the positive rates of the two parameters, alpha2-PAG and carcinoembryonic antigen (CEA). (Author abstract) (26 Refs)

35. IMMUNE COMPLEXES IN OVARIAN CANCER.

Clayton LA, Gall SA, Dawson JR, Creasman WT
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Duke Univ. Medical Center, Durham, NC, 27710
Gynecol Oncol; 13(2):203-212 1982

A polyethylene glycol precipitation (PEG) assay has been used to identify immune complexes in the serum of patients with ovarian cancer. Single radical immunodiffusion was used to quantitate the amount of IgG contained in the immune complexes. This study has shown that significantly higher levels of immune complexes were detected in the serum of ovarian cancer patients with known tumor when compared with ovarian cancer patients who were in remission. Values obtained for patients in remission were within the range of the control group. The levels of immune complexes were also noted to rise before the clinical detection of recurrences or progression of disease. It is therefore suggested that the PEG assay may be a useful marker in patients with ovarian cancer. (Author abstract) (25 Refs)

36. ESTROGEN AND PROGESTERONE RECEPTORS IN TUMORS OF THE HUMAN OVARY.

Hahnel R, Nat R, Kelsall GR, Martin JD, Masters AM, McCartney AJ, Twaddle E
Dept. Obstetrics and Gynaecology, Univ. Western Australia, Subiaco, 6008, Australia
Gynecol Oncol; 13(2):145-151 1982

A total of 23 malignant ovarian tumors and 5 benign or tumor-like lesions of the ovary had their estrogen receptor (ER) status, and of these 15 also had their progesterone receptor (PR) status, determined. Tumors were said to be ER+ when the receptors bound greater than 4 fmole estradiol/mg protein and PR+ when they bound greater than 10 fmole progesterone/mg protein. Ten of 22 ovarian carcinomas were estrogen receptor positive (ER+) and 3 of these also contained progesterone receptors (PR+). All six malignant ovarian tumors occurring in premenopausal women were ER- and PR- as were the two benign tumors occurring in two premenopausal patients. It may be that premenopausal women have tumors which are more frequently ER- PR- because their higher blood hormone levels block the estrogen and progesterone binding sites in the tissues. It was not possible to show any variation from normal in the plasma hormone levels (estradiol, estrone, testosterone, progesterone, FSH). It is suggested that hormone receptor studies of malignant ovarian tumors could aid in the selection of patients suitable for therapies based on endocrine manipulation. (Author abstract) (15 Refs)

37. CHEMOTHERAPY OF ADVANCED OVARIAN CARCINOMA: INITIAL EXPERIENCE USING A PLATINUM-BASED COMBINATION.

Williams CJ, Mead B, Arnold A, Green J, Buchanan R, Whitehouse M
CRC Medical Oncology Unit, Univ. Southampton, Southampton General Hosp., Centre Block CF 93, Southampton SO9 4XY, England
Cancer; 49(9):1778-1783 1982

Thirty-five previously untreated patients with FIGO Stage III or IV ovarian carcinoma were treated with cis-diamminedichloroplatinum (II), Adriamycin and cyclophosphamide (PACe). Following four or five cycles of PACe, patients were assessed clinically for response. Twenty-one (60%) of the patients attained a clinical complete remission (CCR), 7 (20%) a partial remission, and 7 (20%) did not respond. The median survival of all patients was 19 mo, 6.4 mo for partial and non-responders, and 26.5 mo for clinical complete responders. Six patients remain relapse-free for more than 2 yr. Patients entering into the study during the 2nd yr underwent a second-look procedure if they attained a CCR. Ten patients in CCR were assessed for second look; 2 refused, and 8 underwent a laparotomy. Three of eight were in complete remission after second look, and a fourth patient who had microscopic disease in one ovary was rendered free of disease by surgery. Subjective toxicity was marked due to severe nausea and vomiting. Renal toxicity was not troublesome and myelosuppression was moderate. Ototoxicity and peripheral neuropathies were seen in seven patients. PACe is a highly effective induction regime but randomized studies are required to show that improved survival will result from its use. (Author abstract) (18 Refs)

38. KINETIC STUDY OF CIS-DIAMMINODICHLOROPLATINUM IN A CASE OF SEROUS CYSTADENOCARCINOMA OF THE OVARY WITH SEVERE RENAL INSUFFICIENCY.

Giudicelli CP, Ricordel I, Josipovici JJ, Falcot J, Renaudeau G, Bassoulet J, Meunier J
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Therapie; 36(6):653-658 1981

A 51-yr-old woman who presented with local-regional recurrence of an ovarian serous cystadenocarcinoma and resultant renal insufficiency due to ureteral compression was treated with four courses of chemotherapy (adriamycin: 40 mg on day 1; VM 26: 50 mg on day 2; 5-fluorouracil: 500 mg on days 3 and 4; cyclophosphamide: 300 mg on days 3 and 4; and cis-diamminodichloroplatinum: CDDP: 15-100 mg on day 5). The kinetics of CDDP elimination were examined. Urinary excretion of CDDP was max during hr 1-6 following injection, with eliminated quantities accounting for 2.5-12.2% of the total dose administered. CDDP tissue binding was max during hr 1 after administration. At autopsy, CDDP concentrations in the liver, right and left kidney, intestine, and tumor were 26.0, 6.10, 3.86, 2.5, and 1.1 ug/g, respectively. Significant (85-90%) and rapid CCDP binding to plasma proteins was observed. Loss of CDDP via vomiting was negligible (0.6%). CDDP administration allowed 7 mo of satisfying survival despite the presence of renal insufficiency. (17 Refs) (In FRE)

39. PHASE II TRIAL OF AMSACRINE (M-AMSA) IN ADVANCED OVARIAN CARCINOMA.

Dombernowsky P, Siegenthaler P, Somers R, Hansen HH
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Eur J Cancer Clin Oncol; 18(1):71-74 1982

A phase II study of 4'-(9-acridinylamino)methanesulfon-m-anisidide (amsacrine, m-AMSA) was carried out in previously treated patients with advanced ovarian carcinoma. The dose of amsacrine was 90 mg/m2 every 3 wk in 34 patients having received prior extensive chemotherapy and/or radiotherapy, and 120 mg/m2 in 5 patients who had previously only received moderate amounts of chemotherapy. Among patients evaluable for response the median number of courses was three (range 2-17). Two patients (5%) experienced complete response for 15+ mo. Leukopenia was the most frequent toxic effect. WBC nadir was 2,700/mm3 (range 1,000-7,300). Other toxic effects were of lesser significance and included thrombocytopenia, anemia, nausea and vomiting. It is concluded that amsacrine has only marginal activity in patients with previously treated ovarian carcinoma. (Author abstract) (18 Refs)

40. MALIGNANT GERM CELL TUMORS IN CHILDREN.

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Dept. Pediatrics - M650, Univ. California Sch. Medicine, San Francisco, CA, 94143
Front Radiat Ther Oncol; 16:141-149 1982

A combination of vinblastine, bleomycin, cis-diamminedichloroplatinum(II), actinomycin D, adriamycin, and cyclophosphamide was given to 17 children with ovarian germ cell tumors and 12 children with germ cell tumors of other sites excluding testicular. Second-look surgery was performed after the first 18 wk of chemotherapy, which was continued for a total of 102 wk. Radiotherapy was given if second-look surgery disclosed residual disease, before chemotherapy was resumed. All patients showed either complete (CR) or partial tumor regression (PR). The follow-up times were too short for evaluation, but 8/12 patients with nonovarian tumors had no evidence of disease (either at second-look surgery or in follow-up diagnostic imaging and assays of biologic markers) and 13/17 patients with ovarian tumors showed CR. Five patients were still being treated at the time of report and were not yet evaluable. Five patients died with recurrences following either a CR (3/5) or PR (2/5). Three of the patients who died had disseminated or ruptured ovarian tumors at diagnosis. It is concluded that in this decade, the survival rates of children with malignant germ cell tumors may reach 80-90%. (23 Refs)

41. PALMAR FASCIITIS AND POLYARTHRITIS ASSOCIATED WITH OVARIAN CARCINOMA.

Medsger TA, Dixon JA, Garwood VF
Div. Rheumatology and Clinical Immunology, Univ. Pittsburgh Sch. Medicine, 985 Scaife Hall, Pittsburgh, PA, 15261
Ann Intern Med; 96(4):424-431 1982

Six postmenopausal women (ages 50 to 65 yr) developed palmar fasciitis and polyarthritis associated with a malignant ovarian tumor. Rheumatic signs preceded the diagnosis of adenocarcinoma of the ovary by 5 to 25 mo. All had bilateral pain and limitation of motion of the shoulders and hands as well as prominent palmar fasciitis and polyarthritis. Arthritis of the elbows, wrists, knees, ankles, and feet was also common. Two patients had carpal tunnel syndrome. Nonresectable tumor with ascites and peritoneal metastatic seeding was found in all patients. Endometrioid carcinoma, poor tumor differentiation, and unusually severe stromal proliferation of fibrous tissue were seen. There was no consistent improvement of the musculoskeletal syndrome after corticosteroid treatment or chemotherapy. All patients died 2 to 17 mo after diagnosis of the neoplasm. (Author abstract) (44 Refs)

TROPHOBLASTIC DISEASE

42. CLINICAL RESEARCH ON APPEARANCE OF DISEASE AND PATHOLOGY IN PATIENTS WITH TROPHOBLASTIC DISEASES.

Kawashima Y, Yamashita S, Tojo S
Dept. Obstetrics and Gynecology, Kobe Univ. Sch. Medicine, Kobe, Japan
Nippon Gan Chiryo Gakkai Shi; 16(7):1423-1437 1981

During 1971-1978, 2,333 cases of trophoblastic disease (1,989 hydatidiform mole, 153 invasive mole, 70 choriocarcinoma, and 121 undetermined type) were registered in Hyogo prefecture. The rate of occurrences of hydatidiform mole was 2.81/1,000 in the prefecture; of seven regions in the prefecture, people living in the Tajima region had a significantly higher incidence of hydatidiform mole than did those in the other regions. Among the cases of invasive mole, choriocarcinoma, and undetermined-type malignant tumor (94/99, 12/26, and 58/60, respectively) were sequelae of hydatidiform mole. Times required for the development of the sequelae from hydatidiform moles were less than 4 mo for 93/94 invasive moles and was greater than 7 mo for 9/12 choriocarcinomas. Following resection of the hydatidiform moles, malignant sequelae occurred in 291/1,989 cases (144 invasive mole, 34 choriocarcinoma, and 112 undetermined type). Examination of the cases of resected hydatidiform moles which had favorable prognosis showed human chorionic gonadotropin levels of less than 1,000 IU/liter (l) at wk 3, less than 80 IU/l at wk 6, and less than 40 IU/l at wk 8. Cancerous invasion of organs outside of the uterus was observed in 24 cases; invasion of the broad ligament was observed only in cases of invasive mole (7/13), and invasion of the parametrium was observed primarily in cases of choriocarcinoma (4/8). Metastasis was observed in 34/99 cases of invasive mole, 20/26 cases of choriocarcinoma, and 28/60 cases of undetermined-type tumor. During the investigation, 14 patients died (1 invasive mole, 12 choriocarcinoma, and 1 undetermined type); the cause of death in 11/14 was brain metastasis. (20 Refs) (In JPN)

43. CIRCULATING IMMUNE COMPLEXES AS MARKERS OF RESPONSE TO CHEMOTHERAPY IN MALIGNANT TERATOMAS AND GESTATIONAL TROPHOBLASTIC TUMOURS.

Begent RH, Chester KA, Walker LC, Tucker DF
Dept. Medical Oncology, Charing Cross Hosp., London WC2, England
Br J Cancer; 45(2):217-222 1982

Concentrations of circulating immune complexes (CIC) were measured serially during chemotherapy of 22 patients with gestational trophoblastic tumors (GTT) and 11 patients with malignant teratoma (MT) by the polyethylene glycol precipitation and C1q solid-phase assays. Results were correlated with tumor response as measured by serum concentrations of human chorionic gonadotrophin (hCG) and alpha-fetoprotein (AFP). CIC concentrations correlated with disease status in the early stages of treatment in 4/22 patients with GTT and 5/11 with MT. CIC assays were less sensitive than hCG and AFP as a monitor of disease, and also less specific, in that eight patients with GTT and five with MT developed raised CIC concentrations during chemotherapy in spite of sustained complete remission. Measurements of CIC concentrations by present methods are neither sufficiently sensitive nor specific to be of clinical value as a tumor marker in GTT and MT, and this casts doubt on their potential value in other malignancies. Attention should be directed to identification of the components of CIC, some of which may be more cancer-specific. (Author abstract) (25 Refs)

44. PLACENTAL SITE TROPHOBLASTIC TUMOUR (TROPHOBLASTIC PSEUDOTUMOUR): A STUDY OF FOUR CASES REQUIRING HYSTERECTOMY INCLUDING ONE FATAL CASE.

Eckstein RP, Paradinas FJ, Bagshawe KD
(c/o Paradinas) Dept. Histopathology, Charing Cross Hosp. Medical Sch., Fulham Palace Road, London W6 8RF, England
Histopathology; 6(2):211-226 1982

The clinico-pathological features in four patients with placental-site trophoblastic tumor (PSTT) necessitating hysterectomy are presented. Deeply infiltrative tumors were observed; in two patients tumor invaded pelvic organs outside the uterus, and one patient died with metastases despite aggressive chemotherapy and multiple surgery. In the fatal case, possible lung and liver metastases which regressed after chemotherapy were observed with computed tomography (CT). In three patients PSTT behaved as an actively infiltrative tumor resistant to chemotherapy regimes usually effective for choriocarcinoma (CC). Compared with CC cases, serum human chorionic gonadotropin (HCG) levels were relatively low. Histologically the tumors were composed of mononuclear cells supported by a variable amount of vascular stroma; no bilaminar structure such as that seen in CC was observed. Anti-betaHCG and anti-alphaHCG antisera stained scattered cells. Curettage was diagnostic in two cases. Mitotic activity did not correlate with subsequent behavior. Favorable prognostic factors may be inflammatory cell infiltration and evidence of organization around the tumor. The variable behavior of PSTT and the importance of HCG monitoring are emphasized. PSTT must be distinguished from CC, uterine sarcomas, and normal placental site reaction in curettings. Surgical ablation offers the best hope of eradication. The term 'trophoblastic pseudotumor' is not appropriate for such a potentially lethal disease. (18 Refs)

MULTI-SITE STUDIES AND REVIEWS

45. MONOCYTE CHEMOTAXIS IN PATIENTS WITH CERVICAL OR OVARIAN CANCER.

Daunter B, Khoo SK, Mackay EV
Dept. Obstetrics and Gynaecology, Univ. Queensland, Clinical Sciences Building, Brisbane, Queensland, 4029, Australia
Gynecol Oncol; 13(2):152-157 1982

The chemotactic response of peripheral blood monocytes to untreated, complement activated and inactivated autologous serum was determined in patients receiving therapy for cervical or ovarian cancer. A significant reduction in monocyte chemotaxis, based on the number of migrating monocytes, in complement activated autologous serum, was observed in the cervical cancer group relative to the healthy subjects (controls). However, this reduction in response was not reflected in the monocyte chemotactic response index (response in treated serum/untreated serum). No significant difference in monocyte chemotaxis was found between the ovarian cancer group and the controls. (Author abstract) (29 Refs)

46. THE ROLE OF OVARIAN TRANSPOSITION IN CONSERVATION OF OVARIAN FUNCTION IN RADICAL HYSTERECTOMY FOLLOWED BY PELVIC RADIATION.

Hodel K, Rich WM, Austin P, DiSaia PJ
Dept. Obstetrics and Gynecology, Univ. California Irvine Medical Center, Orange, CA, 92668
Gynecol Oncol; 13(2):195-202 1982

Radical hysterectomy is commonly used in treatment of young patients with cervical or vaginal cancer. Adjuvant radiotherapy occasionally is performed following radical hysterectomy in these patients. Nine cases of ovarian transposition in patients undergoing radical surgery followed by pelvic radiation are reported. Dosimetric readings to the transplanted ovaries and post-treatment FSH levels will be discussed. Also reviewed are complications of ovarian transpositions done in patients who did not subsequently receive pelvic radiation. The surgical procedure of ovarian transposition is illustrated. (Author abstract) (6 Refs)

47. GENITAL CANCER AND PRECANCEROUS LESIONS IN WOMEN WITH KIDNEY TRANSPLANTS. A STUDY OF 90 CASES.

Pelissier C, Yaneva M, Joubert E, Peretz M, Rochet Y
Service d'Endocrinologie de la Reproduction, Hopital Necker, 149, rue de Sevres, F 75730 paris, France
Gynecologie; 32(4/5):359-365 1981

A study of benign and malignant genital lesions in 90 women who had undergone renal transplants 3 mo-17 yr previously is reported. Av age at the time of consult for kidney disease was 32.8 yr. Immunosuppressive therapy was given to 89/90 women. One patient who underwent two transplants received total irradiation and thymic irradiation. Two patients were treated for cervical cancer during the time of their dialysis. At follow-up, several cancerous, precancerous, and benign lesions were found. These include one invasive cancer of the uterus, one case of in situ vaginal cancer with degeneration of a viral papilloma, one case of breast cancer, two cases of cervical dysplasia, four cases of moderate dysplasia associated with cervical viral papillomatosis, three viral papillomas, three primary herpetic cervical infections, one case of Bowenoid dysplasia and one case of sclero-atrophic lichen without malignant changes, in the vulva. The papillomatous lesions had not been mentioned in the other seven studies on genital cancer in women with kidney transplants. It is suggested that further studies may elucidate of immunosuppressors in the development of cancerous and papillomatous lesions. (26 Refs) (In FRE)

48. SYNCHRONOUS MULTIPLE PRIMARY NEOPLASMS OF THE UPPER FEMALE GENITAL TRACT.

Matlock DL, Salem FA, Charles EH, Savage EW
(c/o Savage) Dept. Obstetrics and Gynecology, Charles R. Drew Postgraduate Medical Sch., 12021 Wilmington Ave., Los Angeles, CA, 90059
Gynecol Oncol; 13(2):271-277 1982

A case is reported in which there was a simultaneous occurrence of a well-differentiated papillary serous cystadenocarcinoma of the right ovary, a well-differentiated mucinous cystadenocarcinoma of the left ovary, and a rare, moderately differentiated papillary adenocarcinoma with psammoma bodies of the endometrium. A review of the literature failed to reveal the multiple simultaneous occurrence of this particular combination of malignancies of the female genital tract. The diagnosis, histology, and management are discussed. Histogenesis is discussed in relation to theory of area response, to an unknown factor, of embryologically related organs in the development of multiple, multifocal malignancies of the female reproductive system. (Author abstract) (7 Refs)

SELECTED PRE-CLINICAL STUDIES

49. AN ANALYTIC CELLULAR EVALUATION OF ASPIRATED SMEARS FROM TRANSPLANTED HUMAN ENDOMETRIAL ADENOCARCINOMA IN NUDE MICE TREATED WITH 17BETA-ESTRADIOL AND PROGESTERONE.

Ishiwata I, Ishiwata C, Nozawa S, Kurihara S, Okumura H
Ishiwata Obstetrical and Gynecologic Hosp., 1-4-21 Kami-Mito, Mitoshi, Ibaraki-ken 310, Japan
Acta Cytol (Baltimore); 26(2):251-258 1982

The effects of 17beta-estradiol and progesterone on human endometrial adenocarcinomas grafted into BALB/c nude mice were studied. Cytologic studies were made on aspiration biopsy smears obtained from the grafts with a fine needle. Mitotic figures were frequently observed in the cells obtained from 17beta-estradiol-treated mice, whereas there were few mitotic figures in cells from progesterone-treated ones. Progesterone produced such morphologic changes as multinucleolation and cytoplasmic vacuolization. Untreated tumors and those treated with 17beta-estradiol were solid and were interpreted as poorly differentiated adenocarcinomas. Progesterone-treated tumors were slightly soft but were also interpreted as poorly differentiated adenocarcinomas; however, central necrosis was seen frequently, and differentiation occurred at the margin of these tumors. 17beta-estradiol promoted increased tumor growth, whereas progesterone produced differentiation and inhibited tumor growth. (Author abstract) (18 Refs)

50. HUMAN GYNECOLOGIC CANCERS HETEROTRANSPLANTED INTO ATHYMIC NUDE RATS.

Sawada M, Matsui Y, Hayakawa K, Nishiura H, Okudaira Y, Taki I
Div. Gynecology, Dept. Clinical Res., Res. Inst. Microbial Diseases, Osaka Univ., Osaka, Japan
Gynecol Oncol; 13(2):220-228 1982

The serial transplants of human ovarian and endometrial tumors in nude mice were transplanted into nude rats. The transplants consisted of three lines of yolk sac tumors, designated a YST-1, YST-2, and YST-3 and two lines of endometrial adenocarcinoma, AD-30 and AD-35. The transplanted tumors grew much larger in nude rats than in nude mice, reaching more than 150 g in wt. The overall grafting success rate of these tumors was about 70% in nude rats whereas it had been almost 100% in nude mice. The histology of the transplanted tumor in nude rats was similar to that of the same tumor in nude mice. YST-1, YST-2, and YST-3 tumors produced the marker alpha-fetoprotein (AFP). Thus the transplanted tumors in nude rats seemed to preserve the characteristics of the original tumors. The usefulness of the nude rat as a tool for studying the efficacy of treatments on human malignant tumors is discussed. (Author abstract) (9 Refs)

51. THE NATURE OF TROPHOBLASTIC DISEASE INITIATED BY TRANSPLANTATION INTO IMMUNOSUPPRESSED ANIMALS.

Kuto M, Tanaka K, Takeuchi S
(c/o Takeuchi) Dept. Obstetrics and Gynecology, Niigata Univ. Sch. Medicine, 1 Asahimachi-Dori, Niigata, Japan
Am J Obstet Gynecol; 142(5):497-505 1982

To elucidate the nature of trophoblastic disease, trophoblastic tissue was transplanted into nu/nu mice and immunosuppressed Syrian hamsters. All tissue was successfully transplanted, with no tumorigenicity shown in either the 21 cases of hydatidiform mole (HM) or the 10 cases of invasive mole (IM). However, in seven of the nine cases of choriocarcinoma (CC), tumorigenicity was demonstrated by successful serial transplantation. Thus, the conclusion was that CC was clearly a malignant neoplasm, whereas IM and HM should be considered to be benign disease because of their cellular behavior, which was clearly distinct from that of CC in this series. (Author abstract) (14 Refs)

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VAGINAL TUMORS

1. LASER THERAPY OF VAGINAL INTRAEPITHELIAL NEOPLASIA.

Capen CV, Masterson BJ, Magrina JF, Calkins JW
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Kansas Univ. Medical Center, Kansas City, KS, 66103
Am J Obstet Gynecol; 142(8):973-976 1982

Laser therapy of gynecologic neoplasia is relatively new and there is minimal experience with vaginal intraepithelial neoplasia. Fifteen unselected patients with vaginal intrsepithelial neoplasia were treated primarily with the carbon dioxide laser. The av follow-up is 15 mo. At this time there have been two failures and two patients are currently being treated. Eleven patients treated with the laser have no evidence of disease. Guidelines for treatment as well as risk of failure are discussed. (Author abstract) (7 Refs)

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CERVICAL AND UTERINE TUMORS

2. THE IMPORTANCE OF COMPUTED TOMOGRAPHY FOR THE DIAGNOSIS OF TUMORS OF THE UTERUS AND RECURRENT LESIONS.

Steinbrich W, Rohde U, Friedmann G
Radiologisches Institut und Poliklinik, Universitat Koln, Joseph-Stelzmann-Strasse 9, D-5000 Koln 41, W. Germany
Radiologe; 22(4):154-161 1982

The value of computed tomography (CT) in diagnosis of uterine tumors was assessed in 496 patients, including 190 with primary carcinomas and 306 with suspected recurrence of carcinoma. CT was performed using overlapping sections extending from the perineum to the promontory. CT was extended to the retroperitoneum up to the level of the diaphragm to detect lymph node metastases. In pretherapeutic studies cervical carcinoma was demonstrated by CT in 140/159 cases. All 19 false negative findings were obtained with tumors of Stage I or IIa. Tumors included 15 Stage I, 50 Stage IIa, 48 Stage IIIa, 39 Stage IIIb, and 14 Stage IV tumors. Correct staging was obtained by CT in 19/24 cases in which surgical findings were obtained and in 92/135 cases treated by radiotherapy. Pretherapeutic CT examination detected 23/31 tumors. Extrauterine extension of tumor was demonstrated in five cases. Recurrences were detected among 198 patients with prior cervical carcinoma and 26 among 108 with prior endometrial carcinoma. The av interval between initial treatment and detection of recurrence was 14.7 mo for cervical carcinoma and 13.5 mo for endometrial carcinoma. CT detected recurrences in 67/71 patients with cervical carcinoma and 24/26 patients with endometrial carcinoma. With both tumor types false-positive findings resulted from scar formation after radiotherapy. CT findings were useful in cases of primary tumors only for determining the extent of advanced tumors. Detection of lymph node metastases depended on the size of the nodes. CT was useful in examination for recurrence of tumor. (31 Refs) (In GER)

3. UTERINE PAPILLARY SEROUS CARCINOMA. A HIGHLY MALIGNANT FORM OF ENDOMETRIAL ADENOCARCINOMA.

Hendrickson M, Ross J, Eifel P, Martinez A, Kempson R
Dept. Pathology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Am J Surg Pathol; 6(2):93-108 1982

Of 256 cases of Stage I uterine adenocarcinoma, 26 were uterine papillary serous carcinomas (UPSC). Cytological examination of UPSC revealed marked nuclear pleomorphism, hyperchromatic bizarre nuclear 'giants', macronucleoli, and mitotic figures that were frequent and often abnormal. The ages of patients with UPSC ranged from 40-86 yr with a mean of 66 yr. These patients generally presented with abnormal uterine bleeding. All women with UPSC were postmenopausal, and 25% were nulliparous. Patients with UPSC accounted for 50% of the relapses in the total group of Stage I carcinomas. Of the 26 patients with UPSC who were followed, only 4 survived without evidence of disease: one with deeply invasive Stage I disease, two with Stage II UPSC, and one with Stage III disease because of microscopic fallopian tube involvement. Eleven of the UPSC group of patients presented or relapsed with upper abdominal carcinomatosis. When compared with a group of 98 nonpapillary pathologic Stage I patients whose tumors were Grade II or III, the relapse-free survival curve for the UPSC patients is evidence of the adverse prognosis that is attached to the papillary serous type of uterine adenocarcinoma. (28 Refs)

4. GLASSY CELL CARCINOMA OF THE UTERINE CERVIX. AN ULTRASTRUCTURAL STUDY AND REVIEW.

Zaino RJ, Nakhas WA, Mortel R
Dept. Pathology, M. S. Hershey Medical Center, Hersh..., PA, 17033
Arch Pathol Lab Med; 106(5):250-254 1982

Glassy cell carcinoma is an unusual neoplasm of the uterine cervix that accounts for 1% to 2% of all cervical malignant neoplasms. Although it seems to have a distinct histologic appearance, it has generally not been recognized, as indicated by the extremely small number of cases reported in the literature. Previous studies have indicated an aggressive behavior, a poor response to irradiation and surgery, and a tendency to widespread metastases. It occurs in a younger age group (mean age, 41 yr) than other cervical neoplasms and often has been associated with pregnancy. The histogenesis is not known, but electron microscopic examination of one case we studied, and review of one previously described case, demonstrate that it is an adenosquamous carcinoma. The need to define this neoplasm better will be satisfied only by additional, thorough histologic and clinical studies. (Author abstract) (12 Refs)

5. ENDOCERVICAL AND ENDOMETRIAL ADENOCARCINOMA: AN IMMUNOPEROXIDASE AND HISTOCHEMICAL STUDY.

Cohen C, Shulman G, Budgeon LR
Dept. Pathology, Milton S. Hershey Medical Center, Hershey, PA, 17033
Am J Surg Pathol; 6(2):151-157 1982

A retrospective study was conducted of 13 adenocarcinomas of endocervical origin and 21 of endometrial origin with histochemical stains for type and distribution of mucin, and by carcinoembryonic antigen (CEA) immunohistochemistry. All 13 adenocarcinomas of endocervical origin contained CEA, with strongly positive immunostaining in nine. Only 11 of the 21 endometrial adenocarcinomas contained CEA. The degree of tumor differentiation was not correlated with the amount of CEA in either type of adenocarcinoma. Mucicarmine and alcian blue (AB)-positive mucin was present in 12/13 of the endocervical lesions and in 19/21 of the lesions of endometrial origin. Both poorly and moderately differentiated endocervical carcinomas contained large amounts of mucin; with endometrial carcinomas, the amount of mucin apparently correlated with tumor differentiation: better-differentiated lesions showed more mucus production than poorly-differentiated ones. Although criteria are not absolute, better differentiation of endocervical from endometrial carcinoma may be obtained by histochemical staining for the amount, distribution, and type of mucin, and the demonstration of the amount and distribution of CEA. (19 Refs)

6. THE DETECTION OF ESTROGEN RECEPTORS IN GYNECOLOGIC TUMORS USING IMMUNOPEROXIDASE AND THE DEXTRAN-COATED CHARCOAL ASSAY.

Farley AL, O'Brien T, Moyer E, Taylor CR
(c/o Taylor) Dept. Pathology, Univ. Southern California, 2025 Zonal Ave., Los Angeles, CA, 90033
Cancer; 49(10):2153-2160 1982

The dextran-coated charcoal receptor assay for demonstrating functional estrogen and progesterone receptors was used to evaluate the receptor content of gynecological tumors. An immunocytochemical method, the immunoperoxidase antiperoxidase method, that may detect estrogen receptors, was also em-

ployed on the same specimens utilizing sections from formalin-fixed paraffin embedded blocks. The results by the two methods were compared and were correlated with the state of differentiation of the tumors. According to the dextran-coated charcoal method, two cases of well differentiated endometrial adenocarcinoma were strongly positive for both estradiol and progesterone receptors, and three moderately differentiated cases contained lesser amounts of both types of receptors. Six cases of undifferentiated adenocarcinoma ranged from no detectable receptors to very high values, while of five cases of squamous cell carcinoma of the cervix, only two were positive for estradiol receptors by the dextran-coated charcoal method. Staining of tissue sections from these same cases using the immunoperoxidase method, demonstrated a positive correlation to the dextran-coated charcoal assay for estrogen receptors. The Dextran-coated charcoal method is presently being used clinically as a screening measure for statistical probability of a patient's response to hormone therapy. The degree of positive correlation shown here suggests that use of the immunoperoxidase method may have further potential for diagnostic and clinical use, and merits further investigation. (Author abstract) (25 Refs)

7. BLEOMYCIN-MITOMYCIN C IN RECURRENT CARCINOMA OF THE UTERINE CERVIX.

Trope C, Simonsen E, Johnsson JE, Sigurdsson K
Onkologiska kliniken, Lasaretter, S-221 85 Lund, Sweden
Lakartidningen; 79(17):1689-1691 1982

Thirty-three patients (median age 57.5 yr) with inoperable recurrence of carcinoma of the uterine cervix were subjected to chemotherapy with the combination of bleomycin (5 mg/day in iv infusion, days 1-7) and mitomycin C (10 mg on day 8, iv injection). All patients were administered five courses at 7-day intervals. None of the patients had been pretreated with cytostatics, and 32/33 had been irradiated. Irradiation had produced remissions with a median duration of 14 mo. Five of the 33 patients achieved complete remissions and 7/33 partial remissions. No change was seen in 9/33 patients, progressive disease in 12/33. The median duration of complete remission was 12 mo, that of partial remission 6 mo and that of stationary disease 5 mo. The median survival times were 28+ for the patients who achieved complete remission, 10.5 mo for partial remission, 9.6 mo for those who showed no change and 7.6 mo for those with progressive disease. Severe bone marrow depression occurred in 9/33 patients. One patient died of thrombocytopenia. Three patients developed pulmonary fibrosis and one of them died of respiratory failure. (6 Refs) (In SWE)

8. PALLIATION OF ADVANCED RECURRENT PELVIC MALIGNANCIES BY SELECTIVE INTRA-ARTERIAL (IA) COMBINATION CHEMOTHERAPY (MEETING AESTRACT)

Kavanagh JJ, Rutledge FN, Wharton J, Wallace S, Chuang V, Bodey G, Freireich E, Barnes B
M. D. Anderson Hospital and Tumor Institute, Houston, TX, 77030
Proc Am Soc Clin Oncol; 1:C-424 1982

We initiated a pilot study on selective arterial infusions of combination chemotherapy. Duration of infusions range from 72 to 96 hours with 21 to 28 day (D) cycles. Common iliac or internal iliac arteries are infused unilaterally or bilaterally, based on computerized tomographic and angiographic appearance of the tumor. Nuclear medicine perfusion scans are done to assess vascular flow. In cases of shunting to the buttocks, the gluteal artery is occluded. Bilateral internal iliac perfusions receive doses depending on relative contribution of each artery to pelvic flow. Three patients with squamous cell carcinoma of the cervix received systemic Vincristine (2mg) and IA Bleomycin (15-20mg/m(2)-24 hrs), Mitomycin (10mg/m(2)-4 hrs), and cis-Platinum (100-110mg/m(2)-48 hrs) via internal iliac arteries. All patients have cessation of vaginal bleeding. Two have improvement in pelvic pain and one a partial remission. A DES (diethylstilbestrol)-related clear cell carcinoma of the cervix has stopped bleeding and undergone partial remission after two courses with FUDR (deoxyfluorouridine) and P, with planned pelvic exenteration. A recurrent mixed mesodermal sarcoma is stable after one course of Adriamycin and DTIC (dacarbazine). A patient with cloacogenic carcinoma has had pain improvement and less than partial remission after two courses of FUDR and P. (no Refs)

9. CHEMOTHERAPY OF ADVANCED ENDOMETRIAL CARCINOMA WITH PLATINUM, ADRIAMYCIN, AND CYCLOPHOSPHAMIDE (PAC) (MEETING ABSTRACT)

Turbow MM, Thornton J, Ballon S, Koretz MM, Tarti FM
Northern California Oncology Group, Palo Alto, CA, 94304
Proc Am Soc Clin Oncol; 1:C-420 1982

Patients with recurrent or widespread endometrial cancer who had not received prior cytolytic chemotherapy were treated with PAC. All drugs were administered IV:platinum 60mg/M2, adriamycin 50mg/M2, cyclophosphamide 600mg/M2. The treatment was repeated every 3-4 weeks and continued until disease progression. Twenty patients are evaluable for response; 11 no response, 7 partial response, 2 complete response. One patient underwent 2nd-look surgery after 1 year of therapy, and no evidence of residual cancer was found. The median duration of response is 8+ months with 2 patients responding longer than 18 months. Four patients are still on therapy. Ten patents had disease localized to 1 site (pelvis-abdomen); 6 had 2 sites of disease; 4 patients had 3 or 4 sites of involvement. Response was seen only in patients with good Karnofsky Performance Status (KPS) of 80-100%. None of the patients with KPS 50-70% responded to PAC. All 4 of the patients with no prior radiation or chemotherapy responded to PAC. Three of the 5 patients who had received radiation therapy only without any hormone therapy responded. Only 2 of the 11 patients who had received prior hormone therapy responded. Histological grade, amount of residual disease, or number of involved sites did not influence response. Toxicity was as expected: all patients experienced nausea and vomiting. Severe myelosuppression was encountered in 9 patients, and 1 patient developed cardiac toxicity. PAC chemotherapy is effective against endometrial cancer. (no Refs)

10. HIGH RESPONSE RATE WITH COMBINATION CHEMOTHERAPY FOR ADVANCED ENDOMETRIAL CARCINOMA (MEETING ABSTRACT)

Bayer GK, Koch PD
Green Bay Oncology, 835 South Van Buren St., Green Bay, WI, 54301
Proc Am Soc Clin Oncol; 1:C-470 1982

Treatment of advanced endometrial carcinoma remains unsatisfactory. Hormonal therapy has been a standard with a 33% response rate. In Nov 1979 we initiated a pilot study of 11 pts with stage IV disease: day 1-14 cytoxan 100 mg/M2 po, day 1 and 8 5-FU (5-fluorouracil) 500/M2 IV, day 1 cis-diaminedichloroplatinum (DDP) 60 mg/M2 IV. Cycles were repeated every 28 days. Forced saline hydration for 6 hr prior to DDP was achieved and continued for 24 hr. Median age 60 yr, 4 had previous hormonal and chemotherapy. Of the 11 pts, 5 had

pulmonary metastases, 2 pulmonary and abdominal, 4 abdominal-liver-or bone. Two patients had non-measurable disease and remain in remission 98+ and 462+ days. Of 9 with measurable disease, all patients responded, however one is considered a non-responder suffering a pathologic fracture after 2 cycles. There were 3 complete responses and 5 partial responses with median duration of 179+ days. Five patients experienced leukopenia less than 2000 with no episodes of sepsis. Mild to Moderate GI (gastrointestinal) toxicity occurred in all. This regimen is well tolerated with a high response rate. Further testing in a large group should be considered. (no Refs)

11. A RANDOMIZED TRIAL OF THREE CISPLATIN REGIMENS IN SQUAMOUS CELL CARCINOMA OF THE CERVIX (MEETING ABSTRACT)

Bonomi P, Bruckner H, Cohen C, Marshall R, Blessing J, Slayton R
Rush-Presbyterian-St. Luke's, Chicago, IL, 60612
Proc Am Soc Clin Oncol; 1:C-425 1982

The Gynecologic Oncology Group has been conducting a randomized trial comparing three cisplatin regimens, (I) 50 mg/m2 every 21 days vs (II) 100 mg/m 2 every 21 days vs, (III) 20 mg/m2 daily for 5 days every 21 days in women with recurrent or metastatic squamous cell carcinoma. In each regimen cisplatin has been discontinued at a cumulative dose of 400 mg/m2. Five hundred and twelve patients have been entered on this study, and 418 are fully evaluable. Patients excluded from the current evaluation consist of: 22 ineligible, 20 inevaluable, 52 too early to evaluate. The regimens show no difference in progression free interval or survival duration. There is a statistically significant difference in median survival as related to response category: CR (complete response) - median not reached at 12 months, PR (partial response) -9.3 months, no change -8.3 months, progression -3.3 months. Nausea and vomiting occurred in virtually all patients; there was no apparent difference between the three regimens. Other toxicity included: peripheral neurophathy -17 cases, ototoxicity -7 cases. In summary, in treating women with squamous cell carcinoma of the cervix there is no difference in the efficacy of cisplatin given at 50 mg/m2 and 100 mg/m2, and there is less toxicity at the lower dose. (no Refs)

12. PHASE II TRIAL OF CIS-DIAMMINEDICHLOROPLATINUM (DDP) IN TREATMENT OF ADVANCED OR RECURRENT MIXED MESODERMAL SARCOMA OF THE UTERUS (MEETING ABSTRACT)

Thigpen T, Shingleton H, Homesley H, Blessing J
Institute of Mississippi, Jackson, MS, 39216
Proc Am Soc Clin Oncol; 1:C-427 1982

Thirty-six patients with advanced or recurrent mixed mesodermal sarcomas (MMT) of the uterus were entered onto study to receive cis-diamminedichloroplatinum (DDP) 50mg/M2 IV every 3 weeks with vigorous hydration before and after drug administration. Of these 36 patients with MMT, 3 either had no evidence of tumor or another cell type on pathology review, while 2 were never treated, 2 were too early to evaluate, and one was inevaluable for response. Of the 28 evaluable patients, all had had extensive prior therapy (surgery-27; radiotherapy-12; hormones-3; chemotherapy-25). Thirteen had disease confined to the pelvis, while 15 had disease outside the pelvis as well. All but one were ambulatory (performance status 0, 1, or 2). Five (18%) developed an objective response (2 complete (CR) and 3 partial (PR), while 16 (57%) demonstrated stable disease for greater than one month. Seven (25%) showed continued progression of disease. Median duration of reponse was 15 months for complete responders (14 and 16 months respectively) and 3 months for partial responders. Both complete responders remain in CR at 21 + and 27 + months respectively, while the median survival for partial responders was 11 + months. Non-responders had a median survival of 4 months (range 1-19 months). No patient demonstrated a leukocyte count of less than 2000, nor a platelet count of less than 50,000. (no Refs)

13. IMMUNOLOGICAL AND CLINICAL RESPONSES OF PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE CERVIX TO ADJUVANT IMMUNOTHERAPY FOLLOWING RADIOTHERAPY.

McLaren JR, Olkowski ZL, Skeen MJ, Benigno B
Emory Univ. Sch. Medicine, Atlanta, GA
Rev Latinoam Oncol Clin; 13(4):15-21 1981

Clinical and immunological responses of cancer patients to stimulation of the immune system following radiotherapy was investigated. No difference in survival time was apparent between the immunotherapy group (BCG and levamisole) and control group for those who survived less than 8 mo, however a longer survival time appears to favor the immunotherapy group. Radiation depressed immuned parameters in the two test groups showed a statistically significant trend toward recovery during the 40 wk post-radiation period. Since 50% of the patient population is still surviving, the effect of immunotherapy on survival in post-radiation patients cannot be fully analyzed. (12 Refs)

14. CONCURRENCE OF MALIGNANT AND BENIGN HETEROLOGOUS MIXED TUMORS OF THE UTERUS.

Waxman M, Boyce JG, Macasaet MM, Lu T
Dept. Pathology, Nassau Hosp., Mineola, NY, 11501
Am J Clin Pathol; 77(5):631-637 1982

A large polypoid uterine mass was composed of two distinct and separate parts: a malignant mixed mullerian tumor (MMMT) and a benign mixed mesenchymal tumor (BMMT). It was considered a collision of two neoplasms rather than a malignant degeneration of the BMMT. Malignant transformation of benign mesenchymal uterine tumors is a controversial concept which is difficult to prove or disprove. Concerning the histogenesis of MMMT it appears, at least in some cases, that they originate not from a single multipotential mullerian cell, but rather from two, a stromal cell and an epithelial cell. It is suggested furthermore, that in certain instances presence of one neoplastic component, eg, adenocarcinoma, can incite proliferation of the second, sarcomatous element of the MMMT. (Author abstract) (21 Refs)

15. GRANULOPOIETIC INHIBITORS EXCRETED IN THE URINE OF A PATIENT WITH UTERINE CANCER AND MARKED LEUKOCYTOSIS.

Ishii Y, Shinoda M, Nara N, Hirashima K, Shikita M
(c/o Shikita), Natl. Inst. Radiological Sciences, Anagawa, Chiba-shi 260, Japan
Exp Hematol; 10(4):315-325 1982

An inhibitor of colony stimulating factor (CSF) was found in normal human urine and in the urine of a patient with uterine cancer and leukocytosis. The amount of inhibitor excreted in the patient's urine was inversely related to the amount of CSF excreted. Since the patient's urine contained the inhibitor in large amounts, it was used for further characterization of the inhibitor. The inhibitor was separated from CSF by DEAE-

cellulose column chromatography, and precipitated by ammonium sulfate at 30-80% saturation. The result of centrifugation of the inhibitor in a NaBr soln of d = 1.21 and extraction of its soln by chloroform suggested that it is not a lipoprotein. Furthermore, it was inactivated by heating at 60 C. Isoelectrofocusing resolved it into two peaks of pI 6.7-8.4 (pI-7 inhibitor) and pI 4.7-5.4 (pI-5 inhibitor), both of which showed an apparent mol wt of 80,000-90,000 upon Sephadex G-100 chromatography. Dose-response relation for CSF in the presence of the inhibitor(s) showed that the action of the inhibitor(s) was not due to specific inactivation of CSF. Both pI-5 and pI-7 inhibitor fractions showed mitogenic activity to mouse spleen cells in culture, and only slightly inhibited [3H]thymidine uptake in the PHA or LPS stimulated spleen lymphocytes. The result suggests that the granulopoietic inhibitor(s) obtained above is not a non-specifically cytotoxic substance(s). (Author abstract) (28 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

16. PROGNOSTIC SIGNIFICANCE OF PATHOLOGY SUBTYPE AND DIFFERENTIATION IN EPITHELIAL CARCINOMA OF OVARY (ECO) (MEETING ABSTRACT)

Dembo AJ, Brown TC, Bush RS, Sturgeon JF
The Princess Margaret Hospital, Toronto, Ontario M4X 1K9, Canada
Proc Am Soc Clin Oncol; 1:C-408 1982

This study was undertaken to clarify the prognostic implications of pathologic subtype and tumor differentiation in ECO. Between April 1971 and December 1978, 821 patients referred to PMH with invasive ECO were eligible for the study of postoperative treatment methods. Histologic material was reviewed in 808 cases by TCB and classified as serous (SER), mucinous (MUC), endometrioid (END), clear-cell (CLR) or undifferentiated (UND), and graded as WD (well differentiated) or PD (poorly and moderately differentiated). Multivariate analysis was performed on survival rates (SR) and relapse-free rates (RFR) using the log-rank method, correcting for stage, residuum and age. Grade was prognostically significant for SER only. Moreover, there was no significant difference in corrected RFR between MUC and END tumors or between SER PD and UND subtypes. The rare CLR subtype was prognostically similar to SER. The following grouping is a more powerful predictor of SR and RFR than either residuum or stage: (1) SER and CLR, WD (2) MUC and END all grades, (3) SER and CLR, PD, and UND. These data are of major importance for the interpretation of treatment results and patient stratification in clinical trials. (no Refs)

17. CEA IN OVARIAN CANCER (MEETING ABSTRACT)

Malkin A, Kellen JA, Malkin DG, Sturgeon JF, Dembo AJ, Reid JG, McCabe EM
Sunnybrook Medical Centre, Toronto, M4N 3M5, Canada
Proc Am Soc Clin Oncol; 1:C-30 1982

The prognostic value of sequential carcinoembryonic antigen (CEA) tests was evaluated in 325 patients with ovarian cancer participating in a clinical trial. The initial CEA was determined within one to three months following surgery and at least four tests extending over six months were performed serially on all patients. We had established previously that CEA estimations are prognostic of survival independent of stage. In the present study, we tried to determine whether sequential CEA estimations are prognostic of recurrence and survival independent of the classical prognostic factors - stage, histopathologic differentiation and amount of residual disease following surgery. The sequential estimations were categorized as to whether the CEA levels were persistently abnormal, normal, rising, falling or variable. Using a log rank analysis, we found that sequential CEA estimations per se are prognostic of recurrence and survival and, when corrected for stage, tumor differentiation and residual disease following surgery remained prognostic of both recurrence and survival. Whether the persistent elevation of CEA reflects the presence of residual disease undetectable by other means or identifies a particularly malignant phenotype remains to be determined. (no Refs)

18. A RANDOMIZED TRIAL OF CYCLOPHOSPHAMIDE (C) PLUS ADRIAMYCIN (A) WITH OR WITHOUT CIS-PLATINUM (P) IN OVARIAN CARCINOMA (MEETING ABSTRACT)

Omura GA, Ehrlich CE, Blessing JA
University of Alabama in Birmingham, Birmingham, AL, 35294
Proc Am Soc Clin Oncol; 1:C-403 1982

Cis-platinum(P) has emerged as a highly active agent in the treatment of ovarian carcinoma. Uncontrolled studies have implied that CAP is more effective than CA. The aim of the present study is to compare these 2 regimens in a prospective randomized trial. Patients with suboptimal stage III or stage IV disease were stratified by performance status and by measurable versus non-measurable lesions and then randomly assigned to C 500 mg/M2 + A 50 mg/M2 +/- P 50 mg/M2 IV q 3 wk X 8. Clinical complete responders (CR) were to have a second look laparotomy at 6 months; those achieving pathologically confirmed CR were to continue C alone for another year, while partial responders (PR) were taken off the treatment phase of the study. Median age for CA equals 55, for CAP equals 56. Performance status was evenly distributed. In 192 evaluable patients with measurable disease, CA has yielded 20 CR + 26 PR/101 versus 40 CR + 25 PR/91 for CAP. Median response durations are 9.5 and 15.0 months respectively. To date, there are no significant differences in frequency of negative second look or survival. Toxicity has been greater with the 3 drug combination but is manageable. Thus, Cis-platinum combination chemotherapy improves short term results in ovarian carcinoma. (no Refs)

19. CIS-PLATINUM (P), ADRIAMYCIN (A), AND HEXAMETHYLMELAMINE (H) VS CYCLOPHOSPHAMIDE (C) IN ADVANCED OVARIAN CARCINOMA - A RANDOMIZED STUDY (MEETING ABSTRACT)

Carmo-Pereira J, Costa FO, Henriques E
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Proc Am Soc Clin Oncol; 1:C-414 1982

Fifty-three evaluable patients (pts) with disseminated ovarian carcinoma (FIGO III or IV), without prior chemotherapy were randomized to receive either a combination chemotherapy consisting of P (40 mg/m2 iv day 1), A (40 mg/m2 iv day 1) and H (150 mg/m2 po days 2-10, to a maximum of 200 mg), of a 4-weekly cycle, or high dose C alone (40 mg/kg) given intravenously intermittently, every 3 weeks. Pretreatment characteristics in both groups of pts, regarding median age at diagnosis, median time from diagnosis to chemotherapy, FIGO stage, histology, differentiation grade, type of surgery residual disease, previous radiotherapy and median performance status, were comparable. Objective responses were seen in 18/27 of

pts receiving C alone, and in 10/26 of pts treated with the combination regimen, this difference being statistically significant. The median duration of objective response and the median survival were greater in the C group, but these differences were not statistically significant. The toxicity of the combination was more severe. It is concluded that there is no therapeutic advantage for this combination schedule over the alkylating agent used alone. (no Refs)

20. OVARIAN CANCER: SCHEDULE MODIFICATION AND DOSAGE INTENSIFICATION OF CYCLOPHOSPHAMIDE, HEXAMETHYLMELAMINE, ADRIAMYCIN, AND CIS-PLATIN REGIMEN (CHAP II) (MEETING ABSTRACT)

Bruckner HW, Cohen CJ, Deppe G, Dhardwaj S, Zaken D, Storch JA, Goldberg J, Holland JF
Mt. Sinai School of Medicine, New York, NY, 10029
Proc Am Soc Clin Oncol; 1:C-416 1982

Patients (Pts) (24) with objective progression during prior chemotherapy were treated with cis-platin(P) 50mg/(2),d1: Cyclophosphamide 500mg/M2,IV d2, Adriamycin 30-50mg/M2, IV d3 and Hexamethylmelamine 150mg/M2, po d4-10-17. Doses were increased to produce limiting nadir WBC (1000-1500) or platelets (90-125,000). CHAP II produced 6 complete response (CR), 7 partial response (PR), 3 minor response, 2 stable disease (SD), 0 progressive disease (PD) (72% CR+PR) in 18 pts with measurable tumors including 3 CR and 3 PR, 3 MR, 2 SD in 11 measurable pts after failure of a P combination. When median follow-up was 7 mos, cumulative disease free survival (DFS) was 75% 13 mos with only 6 PD. Pt characteristics include 50%, performance status 2-3;58% greater than 60yrs; 71% poor differentiation, 67% residual tumor greater than 5cm. Compared to prior secondary regimens including CAP and CHAP, CHAP II improves response rates after failing a P regimen, improves overall response and significantly increases DFS and S. Pts (5) failing to continue treatment due to toxicity are included in all analyses. Two of 3 additional pts with SD, 1 on AP and 1 on CHAP, achieved surgically proven CR on CHAP II. Best response and survival results to date support primary therapy trials of CHAP II. Second responses (55%) after failure of P combinations in the same doses demonstrates a new potential improved further role of P combinations for pts with 'refractory' disease. (2 Refs)

21. COMBINATION CHEMOTHERAPY INCLUDING CIS-PLATINUM IN PREVIOUSLY TREATED PATIENTS WITH ADVANCED OVARIAN CARCINOMA (MEETING ABSTRACT)

Neijt JP, Ten Bokkel Huinink WW, Hamersma E, Van der Burg ME, Van Oosterom AT, Kooyman CD, Van Houwelingen HC, Pinedo HM
Utrecht University Hospital, 3500 CG Utrecht, The Netherlands
Proc Am Soc Clin Oncol; 1:C-417 1982

In July, 1979, the Ovarian Group initiated a randomized trial in patients with advanced epithelial ovarian cancer, who had shown tumor progression during previous treatment consisting of single-agent alkylating chemotherapy. Patients were randomized to receive either AP (adriamycin 35 mg/sqm iv day 1; cis-platinum 50 mg/sqm iv day 1; repeated day 29) or the HAP regimen (adriamycin 35 mg/sqm iv day 1; cis-platinum 50 mg/sqm iv day 1; hexamethylmelamine 150 mg/sqm po days 15-28; repeated day 36). Of the 52 patients who entered the study, 7 were not evaluable for response and 4 not eligible because tumor progression during previous treatment was not proven. Of these 4 patients, 2 achieved a surgically documented complete remission and 2 a partial remission. In the group of 41 evaluable patients, prognostic factors were equally distributed over the treatment groups. Of those receiving AP, 25% (5/20) responded to treatment, and this was the case for 19% (4/21) of those given HAP. Previous response, Karnovsky, age, and interval from diagnosis were not associated with an increased survival time. No significant differences were found between the therapies as to progression-free survival or overall survival. Responders did not survive significantly longer compared with non-responders. In 50% of the cases moderate or severe toxicity was encountered. (no Refs)

22. COMBINATION CHEMOTHERAPY (CT) WITH CIS-PLATINUM (DDP), L-PAM IV AND HEXAMETHYLMELAMIN (HMM) FOR REMISSION INDUCTION IN OVARIAN CANCER. UPDATE OF A PHASE II TRIAL (MEETING ABSTRACT)

Goldhirsch A, Greiner R, Joss R, Dreher E, Sonntag R, Brunner K
Ludwig Institute for Cancer Research, 3010 Bern, Switzerland
Proc Am Soc Clin Oncol; 1:C-421 1982

Twenty patients (pts) with ovarian cancer were treated with a combination of DDP 80 mg/m2 on day 1 (forced diuresis), L-PAM(L-phenylalnine mustard) 12 mg/m2 iv on day 2 and HMM 130 mg/m2 po on days 8-21 q 28 days for 6 cycles. All but 3 pts had had no prior CT. Thirteen had bulky disease at the start of CT and 7 had a residual tumor of 2 cm after operation. Sixteen pts are evaluable for response, 3 are 'too early: (3 cycles) and 1 refused treatment after the 1st cycle. Four of 8 restaged pts (II-look operation) achieved a pathologically-confirmed CR (complete response) (3/4 had bulky disease prior to CT). Four pts had a PR (partial response) (all had bulky disease prior to CT) but complete removal of macroscopic disease was possible in every case. Of the remaining 8 pts, 6 had not yet been staged but had either a clinically objective remission or no evidence of disease. 2 pts had clinical evidence of progressive disease. Median time to progression was 8+ mos (4-14+ mos). Hematologic toxicity was the dose-limiting toxicity: WBC nadir 1,900/mm3. Platelet nadir was 74,000/mm3. There has been 1 probable toxic death. Three responders were selected for whole abdominal radiotherapy for consolidation of remission. In one, radiation could be carried out, while in 2 prolonged thrombocytopenia was the radiation-limiting toxicity. (no Refs)

23. LONG TERM FOLLOWUP OF HAP (HEXAMETHYLMELAMINE, ADRIAMYCIN, CIS-PLATINUM) VS CAP (CYCLOPHOSPHAMIDE, ADRIAMYCIN, CIS-PLATINUM) IN ALKYLATING AGENT RESISTANT ADVANCED OVARIAN CARCINOMA (MEETING ABSTRACT)

Bernath A, Andrews TA, Dixon RH, Gottlieb RJ, Judson SC, Ellison NM, Harvey HA, Lipton A
Geisinger Medical Center, Danville, PA, 17822
Proc Am Soc Clin Oncol; 1:C-428 1982

Fifty women with stage III or IV alkylator-resistant ovarian carcinoma were randomized to receive HAP (hexamethylmelamine 150 mg/M2 po d 2-15, Adriamycin 40 mg/M2 iv d1, and cis-platinum 50 mg/M2 iv d 1) or CAP (cyclophosphamide 300 mg/M2 iv d 1, Adriamycin 40 mg/M2 iv d 1, cis-platinum 50 mg/M2 iv d 1). Cycles were repeated at 28 d intervals, and measureable disease parameters were followed. Second-look laparotomies were performed to document response status where appropriate. At a median followup time of 28 mo, responses in the 50 pts are: HAP 6 CR (complete response), 5 PR (partial

response), 7 Stable, 9 PD (progressive disease); CAP 3 CR, 4 PR, 8 Stable, 8 PD. Objective response rates were 41% (11/27) HAP, and 30% (7/23) CAP. ECOG grade 2 or worse hematologic toxicity was equivalent for the 2 arms (8/23 CAP, 11/27 HAP), but severe, ECOG grade 3 or worse, neurotoxicity requiring discontinuance of the therapy was seen only in the HAP arm (3/27). Prognostic factors including histologic type, grade, tumor bulk, stage, age were well balanced between the groups. Median survival for all pts was 12 mo from d 1; 7.5 mo for HAP, 13.5 mo for CAP. Of the 9 pts alive at 24 mo, 7 are free of disease and off treatment. No relapses have been seen as yet past 24 mo. CAP and HAP seem equivalent in response rates, with CAP being less toxic. Salvage chemotherapy can achieve worthwhile long term remissions in pts who have failed the alkylating agents--normally an exceedingly poor pronostic sign for survival. (no Refs)

24. CISPLATIN (DDP)/CYTOXAN: A HIGH DOSE DDP REGIMEN FOR ADVANCED STAGE OVARIAN CARCINOMA (MEETING ABSTRACT)

Wernz JC, Speyer JL, Neamoff J, Faig D, Clayton M, Muggia F
NYU Medical Center, New York, NY, 10016
Proc Am Soc Clin Oncol; 1:C-435 1982

Alkylating agents and DDP are among the most active agents in ovarian cancer. In an effort to use these agents maximally, 26 previously untreated patients (pts) were treated with the following regimen: 1) surgical debulking when possible, 2) DDP 20mg/m2IV daily x5 and Cytoxan 600mg/m2 on day 4 q 3-5weeks. Median age was 55 (range 22-73y). After six cycles, patients were restaged by noninvasive means and if negative, sequentially with laparoscopy and laparotomy. Pts with residual disease were continued on therapy and restaged after 3 additional cycles. Twenty one pts were Stage III or IV. Of these, 20 completed therapy and 19 are evaluable noninvasively, 7 complete remission (CR), 7 partial remission (PR), and 5 progressive disease (PD). Six of 7 CR were confirmed by restaging laparotomy, 1 pt underwent laparoscopy only. Objective response rate is 74% and CR is 36%. All pts with CR are disease free at a median of 13+ months (mos) from diagnosis. Six of 7 pts with PR are alive at a median of 12+ mos from diagnosis, one expired 8 months from diagnosis. Median survival of pts with PD is 10 mos. Toxicities of this regimen include myelosuppression with 16/25 patients with WBC less than 2,500 and 25% of courses delayed or shortened because of myelosuppression, peripheral neuropathy (15/26 pts), and cumulative mild renal dysfunction (11/26). Anemia requiring transfusions in 13/26 pts and vomiting in 25/26 pts were also common. (no Refs)

25. TREATMENT OF ADVANCED OVARIAN CANCER WITH CIS-PLATIN, ADRIAMYCIN AND CYTOXAN (PAC) (MEETING ABSTRACT)

Budd GT, Livingston RB, Webster K, Reimer R, Martimbeau P, Hewlett JS
Cleveland Clinic Foundation, Cleveland, OH, 44106
Proc Am Soc Clin Oncol; 1:C-455 1982

A retrospective analysis of 42 patients (pts) with Stage III, IV or recurrent epithelial ovarian cancer treated with monthly cis-platin (P), Adriamycin (A) and Cytoxan (C) was made. Initial doses were: P(50-100 mg/M2, A(20-50 mg/M2 and C(400-650 mg/M(2)). Of 36 pts with measurable disease, 18 (50%) achieved a clinical complete response (CR) and 12 (33%) achieved a partial response (PR) for an objective response rate of 83%. Six Stage III pts remained without measurable disease after surgery and post-operative PAC and are included in the survival data. The median survival of all pts was 21 months (10 months for non-responders) with a median duration of response of 15 months (19+ months for CR's). Patients who were in clinical CR at 6 months and who received 6 or fewer courses of cis-platin had a worse survival (30% at 2 years) than those who received more than 6 courses of cis-platin (70% at 2 years). Of 16 pts in clinical CR undergoing second-look laparotomy, 8 were free of disease at surgery. Of these 8 surgical CR's, 2 have suffered isolated CNS relapses while the rest remain free of disease. No pts died as a result of therapy, but 3 suffered life-threatening leukopenia and 7 had severe leukopenia. Life-threatening thrombopenia was noted in 3 pts. Only 2 pts had renal toxicity, and these were subclinical. Paresthesias were noted by 6 pts. (no Refs)

26. WEEKLY CIS-PLATINUM REMISSION 'INDUCTION' AND COMBINATION DRUG CONSOLIDATION AND MAINTENANCE IN OVARIAN CANCER (MEETING ABSTRACT)

Barlow JJ, Piver MS, Lele SB
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Soc Clin Oncol; 1:C-464 1982

Single-agent weekly Cis-Platinum (DDP) has been our most consistently effective chemotherapeutic regimen for the treatment of previous chemotherapeutic failures in patients with advanced stage ovarian adenocarcinomas. This high response rate to weekly DDP is in sharp contrast to our results with 3-4 weekly DDP in similar patients. In the present study we gave weekly DDP to previously untreated patients with Stage III-IV epithelial ovarian cancers as 'induction' chemotherapy. DDP 'induction' with four weekly courses was randomly followed by 5 monthly 'consolidation and maintenance' courses of either high-dose Methotrexate with CF (citrovorum factor) Rescue plus Cytoxan (MECY) or Cytoxan, Hexamethylmelamine, Adriamycin and DDP (CHAD). Sixteen patients have been entered, all but 4 had measurable disease. Twelve patients are evaluable for the effects of DDP alone. Eleven patients are evaluable for DDP plus the combination regimen. After 4 weekly DDP courses (1 mg/kg/week as a six hour infusion) 10/12 (83%) had objective responses, 4 (33%) complete and 6 partial. Subsequent treatment with combination chemotherapy enhanced the responses. Of the 10 objective responders 9 are now complete (82%) and 1 partial of 11 evaluable patients (91%). Responses have lasted for 3-9 months (median 7 mos). Thus far 5/5 complete responses have been confirmed by laparoscopy after 6 months of therapy. (2 Refs)

27. LIMITED RESIDUAL ADVANCED OVARIAN CANCER--A CURABLE NEOPLASM (MEETING ABSTRACT)

Greco FA, Burnett LS, Wolff SN, Hande KR, Richardson RL, Oldham RK, Jones HW
Vanderbilt University Medical Center, Nashville, TN, 37232
Proc Am Soc Clin Oncol; 1:C-412 1982

From August 1977 to February 1980, 71 patients (pts) with advanced epithelial ovarian cancer received a brief, intensive course of chemotherapy including hexamethylmelamine, adriamycin, platinum and cyclophosphamide or 5-fluorouracil. Twenty-four of the 71 pts (34%) had limited residual carcinoma before starting therapy. Twenty-one of the 24 pts attained this status by resection and 3 pts by previous alkeran chemotherapy. The majority of the pts had moderate to high grade tumors, 20 pts were state III, 2 pts stage IV, and 2 pts stage IC. Of the 22 pts with stage III or IV disease, the remaining

residual disease ranged from 0.5-3cm. At 6 months after beginning combination chemotherapy a laparotomy was done in all pts to assess response and to resect residual tumors if necessary. Twenty pts had no tumor identified (complete response), 2 had all known residual tumor resected, and 2 had residual unresectable tumor. Two of the 3 pts who had previously received alkeran obtained a complete response, but both relapsed at 16 and 26 months. Eighteen of the 21 previously untreated pts had a complete response, and 14 of these 18 pts remain free of detectable tumor from 21-44 months. These data highly suggest: 1) aggressive surgical resection to place pts in the limited residual category is indicated before chemotherapy; 2) a short period (6 months) of intensive platinum-based chemotherapy can produce a laparotomy proven complete response in the majority of pts; 3) a substantial portion of pts with limited residual advanced ovarian cancer are curable. (1 Ref)

28. CHANGES OF THE KARYOTYPE OF THE OVARIAN CANCER CELLS AFTER CHEMOTHERAPY.

Irzhanov SI, Serov SF, Neishtadt EL, Gorovitskaia EN, Zel'dovich DR
Res. Inst. Oncology, Leningrad, USSR
Tsitol Genet; 16(1):25-28 1982

The cytogenetic effect of chemotherapy was studied in 62 patients with ovarian cystadenocarcinoma. Analysis of the ascitic fluid showed that administration of the antineoplastic agents caused progressive increase of the number of cells with aberrant metaphases and decrease of the number of cells with the modal chromosome complement. These changes were observed in the paradiploid cells as well as in the paratetraploid cells. (14 Refs) (In RUS)

29. INTRAPERITONEAL IMMUNOTHERAPY OF HUMAN OVARIAN CARCINOMA WITH CORYNEBACTERIUM PARVUM (MEETING ABSTRACT)

Bast RC, Berek JS, Obrist R, Griffiths CT, Berkowitz R, Hacker NF, Parker L, Lagasse LD, Knapp RC
Sidney Farber Cancer Institute, Boston, MA, 02115
Proc Am Soc Clin Oncol; 1:C-150 1982

Direct contact between immunostimulants and tumor cells has favored effective immunotherapy in animal models and clinical trials. In previous studies of a murine ovarian carcinoma, IP administration of C parvum inhibited IP tumor growth and augmented the activity of peritoneal cells for antibody dependent cell mediated cytotoxicity (ADCC). Doses and schedules of C parvum that augmented ADCC also potentiated serotherapy with specific rabbit heteroantiserum. C parvum (0.25-4.0 mg/m(2)) has been administered IP on 1-8 occasions to 11 patients with peritoneal implants of ovarian carcinoma that had failed to respond completely to cytoreductive surgery and combination chemotherapy. An additional 2 patients have been treated in an adjuvant setting following a complete response to chemotherapy. Fifty-one courses of IP immunotherapy have been associated with fever greater than 101 F (25%), abdominal pain (88%), nausea (57%), vomiting (29%) and hypotension (6%). Of 11 patients with residual disease, 8 have been treated for a sufficient period to evaluate response. Among these 8 patients, 2 have had complete responses (5 and 12 mo), 1 a partial response, 2 stabilizaiton of disease and 3 disease progression. Administration of C parvum IP has augmented the ability of human peritoneal cells to lyse human ovarian carcinoma cell lines in the presence of specific rabbit heteroantiserum. C parvum administered IP appears to inhibit the growth of human ovarian carcinoma and may prove useful for modulating the activity of human effectors of ADCC. (no Refs)

30. A REVIEW OF 728 CASES OF OVARIAN TUMOR: WITH PARTICULAR EMPHASIS ON SECONDARY NEOPLASMS (MEETING ABSTRACT)

Kagan AR, Ryoo MC, Tawa K, Saltz A
Department of Radiation Therapy, Southern California Permanente Medical Group, Los Angeles, CA, 90027
Proc Am Soc Clin Oncol; 1:C-401 1982

Between 1956 and 1977, 728 patients with Stages I, II, and III cancer of the ovary were treated and followed for a minimum of 6 months or until death. The majority of patients were treated with surgery, radiation and chemotherapy (80%). The survival rate at 5 years was 70%, 50%, 16% in patients with Stage I, II, and III respectively. Twelve patients developed other primary malignancies after the diagnosis and treatment of ovarian cancer. One patient developed acute nonlymphocytic leukemia two years and ten months after the laparotomy. Expected number of patients to develop second malignancy including acute nonlymphocytic leukemia using the Third National Cancer Study Survey as a control is not increased. (no Refs)

31. OVARIAN STRUMAL CARCINOID AN IMMUNOCYTOCHEMICAL AND ULTRASTRUCTURAL STUDY OF TWO CASES.

Ulbright TM, Roth LM, Ehrlich CE
Dept. Pathology, Indiana Univ. Sch. Medicine, 1100 W. Michigan St., Indianapolis, IN, 46223
Am J Clin Pathol; 77(5):622-631 1982

Examination by immunoperoxidase methods showed that two strumal carcinoids contained thyroxine in the follicular epithelium and colloid. Ultrastructure showed features of thyroid epithelia. Granule-containing cells replaced some follicular epithelial cells at the colloid interface. The morphology of the granules of these cells resembled those of C-cells and foregut-hindgut carcinoids. Transition between thyroid and carcinoid occurred by proliferation of interfollicular cells which subtly formed trabecular structures. Immunoperoxidase for calcitonin was positive both in the interfollicular cells of one tumor and in cells near the transition from thyroid to carcinoid pattern of the other. We conclude that thyroid tissue is a proven component of strumal carcinoid but that follicular epithelial cells may be replaced by granule-containing parafollicular cells. We suggest that the transition from thyroid to carcinoid is accomplished through an intermediate stage of calcitonin-positive cell proliferation. We emphasize, however, that these neoplasms are types of teratomas which may show several forms of differentiation. The tumor of one patient had mid-gut carcinoid elements and represents the first described strumal carcinoid with the carcinoid syndrome. (Author abstract) (21 Refs)

TROPHOBLASTIC DISEASE

32. THE ROLE OF VP16-213 (ETOPOSIDE; NSC-141540) IN GESTATIONAL CHORIOCARCINOMA.

Newlands ES, Bagshawe KD
Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England
Cancer Chemother Pharmacol; 7(2/3):211-214 1982

Addition of VP16-213 to chemotherapeutic regimens for gestational trophoblastic tumors (GTT) is reported. Thirty-seven patients with drug-resistant choriocarcinomas received single

agent VP16-213 [100 mg/square meter (m2) iv on 5 consecutive days]. Radioimmunoassay specific for human chorionic gonadotrophin (HCG) was used to monitor response to therapy. Seven partial responses (PR), 14 improvements (IMP), and 16 non-responses (NR) were seen. Thirty-eight patients with choriocarcinoma considered at medium prognostic risk were treated with VP16-213 in addition to other chemotherapeutic agents (VP16-213, actinomycin D, methotrexate, folinic acid in course 1, and vincristine and cyclophosphamide in course 2); 13 achieved PR and 17 IMP. Currently 30 patients are in complete remission (CR). Use of VP16-213 improved the ease of obtaining a CR and reduced the chances of developing drug-resistant disease compared with drug regimens lacking the drug. An additional 24 patients were considered high risk. VP16-213 alternating with the above-mentioned drugs provided a satisfactory remission rate (16 CR) while significantly reducing the rate of toxicity. VP16-213 should be one of the first line agents in treating patients with gestational choriocarcinoma who are in medium or high-risk prognostic groups. (8 Refs)

MULTI-SITE STUDIES AND REVIEWS

33. FIRST REPORT ON BEHAVIOR OF PHENYLALANINE AND TYROSINE IN SERUM OF PATIENTS WITH GYNECOLOGICAL CARCINOMAS.

Elling D, Bader K, Lenke S, Bartel U, Koch P
Universitats-Frauenklinik, Tucholskystr. 2, DDR-1040 Berlin, E. Germany
Zentralbl Gynaekol; 104(3):175-181 1982

Preliminary results so far obtained from measurement of free amino acids in the serum of patients with gynecological carcinomas are reported in this paper. Particular reference is made, in that context, to rising levels of phenylalanine and tyrosine in the serum of patients with clinically manifest carcinomas. Their possible use as tumor markers is discussed. (Author abstract) (14 Refs) (In GER)

34. PERIPHERAL PLASMA IMMUNOREACTIVE 6-OXO-PROSTAGLANDIN F1ALPHA AND GYNAECOLOGICAL TUMOURS.

Alam M, Jogee M, MacGregor WG, Dowdell JW, Elder MG, Myatt L
Inst. Obstetrics and Gynaecology, Hammersmith Hosp., Du Cane Road, London W12 OHS, England
Br J Cancer; 45(3):384-389 1982

Peripheral plasma levels of immunoreactive 6-oxo-PGF1alpha, the stable hydrolysis product of prostacyclin, were significantly higher in female patients with tumors of the genital tract than in normal controls. In the groups with malignant tumors, these high levels declined after operation and/or radiotherapy if the tumor responded to treatment. In patients who did not respond to treatment or with tumor recurrence, levels of plasma 6-oxo-PGF1alpha remained high or even rose further. Benign gynecological tumors were also associated with significantly raised plasma 6-oxo-PGF1alpha levels, and these fell to normal levels immediately on surgical removal of the tumor. Possible reasons for these alterations are described. Further investigations are warranted to see whether serial measurements of plasma 6-oxo-PGF1alpha could be used as a prognostic index for the clinical status of patients with gynecological tumors. (Author abstract) (18 Refs)

35. CARCINOMATOUS MENINGIOSIS DURING CIS-PLATINUM TREATMENT OF GYNECOLOGICAL CANCERS.

Kaufmann M, Zalounais M, Rabe T, Heiarich D, Kubli F
Universitats-Frauenklinik Heidelberg, Voostr. 9, 6900 Heidelberg 1, W. Germany
Geburtshilfe Frauenheilkd; 42(3):166-168 1982

Two cases of carcinomatous meningiosis are reported. One occurred during cis-platinum combination treatment (PAC-scheme) for advanced ovarian carcinoma and one during the same treatment for a carcinoma of the cervix. Both patients showed no neurological problems prior to chemotherapy. The central nervous symptoms developed rapidly following the administration of small doses of cis-platinum (total dose 160 or 300 mg) and could not be controlled. In one case tumor cells were found in the cerebral spinal fluid. The cause of death could have been an unusually toxic reaction to cis-platinum. A thorough neurological examination prior and during chemotherapy with cis-platinum is necessary in order to recognize toxic side effects of the drug as soon as possible. (Author abstract) (18 Refs) (In GER)

36. EFFECTIVE THERAPY FOR MALIGNANT GERM CELL TUMORS IN CHILDREN: A STUDY BY THE CHILDREN'S CANCER STUDY GROUP (MEETING ABSTRACT)

Ablin A, Ramsay N, Krailo M, Adkins J, Isaacs H, Deutsch M, Hays D, Exelby P, Grosfeld J, Leikin S, Hammond D
Children's Cancer Study Group, Los Angeles, CA, 90031
Proc Am Soc Clin Oncol; 1:C-419 1982

Fifty-four children were registered on a multi-drug program for the treatment of malignant germ cell tumors (MGCT) of all sites except testes and brain. Germinomas and teratomas with immature and embryonal elements were excluded. Initial surgery was followed by chemotherapy with vinblastine, bleomycin, cis-platinum, actinomycin, cytoxan and adriamycin. Second look surgery was performed at 18 weeks and radiation therapy was given only to those patients with residual disease at second look surgery. Chemotherapy was continued for 102 weeks. Of the 30 patients with ovarian MGCT; 20 are evaluable with a median time on study of 11 months. The initial stage of patients with ovarian MGCT was Stage I-4, Stage II-1, Stage III-12, and Stage IV-3. Nineteen (95%) achieved a complete remission (CR) with chemotherapy and/or surgery and 1 a partial remission (PR). Four of 19 patients who achieved a CR developed progressive disease (PD) 2-23 months after achieving CR and 3/4 have died. Of the 24 non-ovarian patients, 18 are evaluable with a median time on study of 10 months. The sites were: sacrococcygeal (9), mediastinal (4), paraspinous (1), abdominal (1), inguinal canal (1), cervix (1), unknown (1). Ten had metastatic disease and 8 had local or regional disease at diagnosis. Ten (56%) achieved CR; 6 (33%) PR and 2 are too early in treatment. Five of 6 patients who were PR developed PD and of those 2 have died. (no Refs)

37. GENITAL TRACT TUMORS IN CHILDREN.

Breen JL, Bonamo JF, Maxson WS
Dept. Obstetrics and Gynecology, St. Barnabas Medical Center, Livingston, NJ, 07039
Pediatr Clin North Am; 28(2):355-367 1981

The most common type of gynecologic tumor in children less than 15 yr of age is ovarian neoplasm, but it only accounts for about 1% of all malignant neoplasms in girls less than 17 yr of age. Germ cell tumors account for 58-67% of pediatric

ovarian neoplasms and are more likely to be malignant the younger the patient. Diagnosis and treatment of malignant and nonmalignant lesions of the vulva, uterus, and cervix are reviewed. The importance of correct diagnosis followed by individualized therapy which preserves reproductive and menstrual function is stressed. (32 Refs)

38. SCREENING OF ADOLESCENTS EXPOSED TO DIETHYLSTILBESTROL IN UTERO.

Bibbo M, Gill WB
5841 S. Maryland Ave., HM 449, Chicago, IL, 60637
Pediatr Clin North Am; 28(2):379-388 1981

Guidelines for the examination of both male and female adolescents exposed in utero to diethylstilbestrol (DES) are presented. Conditions to be considered in screening of females include clear-cell adenocarcinoma of the vagina and cervix, squamous neoplasia, benign abnormalities of the vagina and cervix, uterine corpus and tube anomalies, and fertility problems. Reported abnormalities in DES-exposed males include epididymal cysts, undescended testis, hypoplastic testis, penile urethra problems, and infertility. Both diagnostic and therapeutic procedures are outlined. (41 Refs)

SELECTED PRE-CLINICAL STUDIES

39. CYTOTOXICITY ON TUMOR CELLS OF HUMAN MACROPHAGES: FUNCTIONAL STATUS OF TUMOR-ASSOCIATED EFFECTOR CELLS.

Mantovani A, Bordignon C, Biondi A, Introna M, Allavena P, Tedesco, Ruco L
Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62, 20157 Milan, Italy
Adv Exp Med Biol; 141:99-108 1982

Tumoricidal activity of human mononuclear phagocytes is reviewed. The nonspecific cytotoxicity of macrophages isolated from ascitic and solid ovarian tumors was measured using TU5 tumor cells as targets. Blood monocytes from ovarian cancer patients had cytolytic activity somewhat lower (p less than 0.01) than control effectors, although there was wide overlap between the two groups when the capacity of monocytes to mature into macrophages was taken into account. Various stimuli such as interferon (IF), lymphokines and endotoxin augmented the cytotoxicity of tumor-associated macrophages (TAM). In a few patients macrophages from the ascitic and solid neoplasm showed similar activation of TAM, whereas TAM from two additional solid tumors were less responsive than effectors from ascites. In an effort to further investigate the tumor-host relationship at the tumor site, the susceptibility of primary ovarian carcinoma cultures to macrophage cytotoxicity was investigated. Ovarian tumor cells from different donors were heterogeneous in their interaction with mononuclear phagocytes. Some tumor cells were resistant to lysis by unstimulated effectors. Growth of these macrophage-resistant tumor cells was usually stimulated by macrophages. A similar heterogeneity of susceptibility was observed when IF or lymphokine stimulated effectors were used. (37 Refs)

40. DEFECTIVE NK ACTIVITY OF HUMAN OVARIAN TUMOR-ASSOCIATED LYMPHOID CELLS: LOW NUMBERS OF EFFECTORS ARE PRESENT IN SITU (MEETING ABSTRACT)

Allavena P, Introna M, Colombo N, Mantovani A
Istituto di Ricerche Farmacologiche, Mario Negri, Milano, Italy
Fed Proc; 41(3):599 1982

This study was designed to elucidate the mechanisms involved in the defective NK (natural killer) activity of tumor-associated lymphocytes (TAL) in human ovarian carcinoma. Lymphoid cells were separated from 15 ascitic and 2 solid tumors on discontinuous Ficoll-Hypaque. NK activity was measured against K562 target cells in a 4 or 20 hr 51Cr release assay. Purified preparations of TAL usually had low levels of NK activity compared to autologous peripheral blood lymphocytes (PBL). NK effector cells in the blood have been morphologically identified as large granular lymphocytes (LGL). It was, therefore, of interest to evaluate the % LGL in the TAL and PBL of these patients. Purified TAL had a very low number of cells with LGL morphology (median 2%, range 0.1-10) while PBL had 10% median LGL (range 5-20). Percoll fractionated TAL and PBL gradients resulted in an enrichment of LGL in the lower density bands up to 40% in the TAL population, and 70-80% in the PBL. NK activity from PBL and TAL was also recovered in the low density cells and was 2-4 fold increased compared to the input populations. These data indicate 1) a positive correlation between LGL and NK activity also at the tumor site; 2) a low frequency of the relevant effector cells (LGL) is one of the major factors involved in the defective NK activity within human ovarian carcinoma. (no Refs)

41. INTERFERON EFFECT ON CYTOTOXICITY OF PERIPHERAL BLOOD AND TUMOR-ASSOCIATED LYMPHOCYTES AGAINST HUMAN OVARIAN CARCINOMA CELLS.

Allavena P, Introna M, Sessa C, Mangioni C, Mantovani A
(c/o Mantovani), Istituto di Ricerche Farmacologiche 'Mario ONegri', via Eritrea 62, 20157 Milan, Italy
JNCI; 68(4):555-562 1982

A study was done to investigate the tumoricidal activity of peripheral blood lymphocytes (PBL) and tumor-associated lymphoid cells (TAL) against freshly isolated tumor cells in human ovarian carcinoma. TAL and carcinoma cells were purified by density and velocity sedimentation on discontinuous Ficoll-Hypaque gradients and fetal bovine serum. Purified carcinoma cells from 23 ascitic and 3 solid tumors were used as targets in a 4-or a 20-hr 51Cr release assay. K562 cells were used to measure natural killer (NK) activity. Freshly purified ovarian carcinoma cells were relatively resistant to lysis by normal unstimulated PBL. Cytolytic activity of ovarian cancer PBL and TAL did not exceed that of control PBL; only one PBL preparation had high levels of cytotoxicity (36.2 and 42.9% specific lysis after 4 and 20 hr at an effector-to-target cell ratio of 50:1) against autologous cancer cells but not against allogeneic targets (less than 5% specific lysis). TAL and, to a lesser extent, ovarian cancer PBL showed impaired NK activity against K562 compared to the activity seen in controls. In vitro exposure to partially purified human fibroblast interferon (IFN; 1,000 U/ml for 1-18 hr) augmented NK activity against K562 of PBL and TAL. When ovarian carcinoma cells were used as targets, IFN enhanced the cytotoxicity of normal PBL in a 4-and 20-hr assay; stimulation by IFN was less frequently observed with ovarian cancer PBL and

TAL in a 4-hr assay, but after 20 hr effector cells from tumor-bearing subjects showed IFN-boosted cytotoxicity against carcinoma cells similar to the degree of cytotoxicity seen in controls. IFN enhanced the cytotoxicity of PBL and TAL against both autologous and allogeneic carcinoma cells. Thus PBL and TAL are rarely cytotoxic against 51Cr-labeled fresh autologous carcinoma cells, but in vitro exposure to IFN induced low levels of killing of ovarian tumor cells. (Author abstract) (18 Refs)

42. INHIBITORY FACTOR (IF) IN OVARIAN CANCER PATIENT ASCITIC FLUID INTERFERES WITH BINDING OF ANTIBODY TO TUMOR ANTIGEN NB/70K (MEETING ABSTRACT)

Knauf S, Beecham J
University of Rochester Medical Center, Rochester, NY, 14642
Fed Proc; 41(3):413 1982

While we were attempting to purify human ovarian tumor antigen NB/70K from malignant ascitic fluid from ovarian cancer patients, an inhibitory factor was discovered and purified to a high specific activity as compared to the original ascitic fluid. 125I-labelled IF does not bind to anti NB/70K, but unlabelled IF decreases the binding of radiolabelled fraction OCC (source of NB/70K) to anti NB/70K. Such results indicate that IF attaches to NB/70K and prevents NB/70K from binding to antibody. Analysis of NB/70K-anti NB/70K, NB/70K-anti IF, and IF-anti IF immune complexes supports this conclusion. Treatment of labelled or unlabelled IF with neuraminidase does not decrease the inhibition of the NB/70K radioimmunoassay or increase the binding of radiolabelled IF to anti NB/70K, indicating that IF and NB/70K are not related as sialo- and asialo- forms of the same antigen. IF is soluble in both 50% saturated ammonium sulfate and 0.6 M perchloric acid, binds to Con-S-4B, and is non-dialyzable, all properties shared with NB/70K. In addition, the acrylamide gel mobility of radiolabelled IF is similar to that of one band (not the NB/70K band) of fraction OCC both before and after neuraminidase treatment. (no Refs)

43. IMMUNOLOGIC ANALYSIS OF GLYCOPROTEINS RELEASED TO CULTURE MEDIUM IN VITRO BY HUMAN OVARIAN CARCINOMA CELLS (MEETING ABSTRACT)

Johnson EA, Piver MS, Gamarra M, Allen HJ
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:994 1982

We have begun an immunologic analysis of glycoproteins released by human ovarian carcinoma cells. Mucinous (Mu), Serous (Se), serous-endometroid (S-E) and clear cell (CC) adenocarcinoma cell clusters were isolated from effusions and incubated without protein supplement to generate antigen(s). The following antisera gave no reaction with culture medium components by immunodiffusion: anti-haptoglobulin, -alpha2-macroglobulin, -beta2-microglobulin, -fibrinogen, alpha-lipoprotein, -beta-lipoprotein, -fibronectin, -secretory component, -IgA, -IgM and -alpha1-acid glycoprotein. Anti-whole serum reacted with culture medium from Mu, S-E, CC and Se adenocarcinoma cells. Rabbit anti-globulin, - [IgG+IgA+IgM] and -IgG reacted with S-E and CC as did goat anti-[IgG+IgA+IgM]. Mu, S-E, Se and CC showed reaction of identity when tested against anti-Mu, -S-E, -Se, and -normal ovary (NO). Anti-Mu, -S-E, -Se, and -NO showed a reaction of identity with each culture medium. Immunoprecipitation experiments with metabolically labeled culture medium and iodinated (125I) pooled NO extract also demonstrated antigenic cross-reactivity. Commercial goat anti-CEA precipitated labeled glycoproteins whereas colon carcinoma-specific rabbit anti-CEA did not. These data indicate that ovarian carcinoma cells of different histologic types release a common antigen in vitro which is also present in normal ovary. The CEA released appears related to but not identical with colon CEA. The reactivity with anti-immunoglobulin (Ig) could be due to specific adsorption in vivo and release of Ig in vitro. (no Refs)

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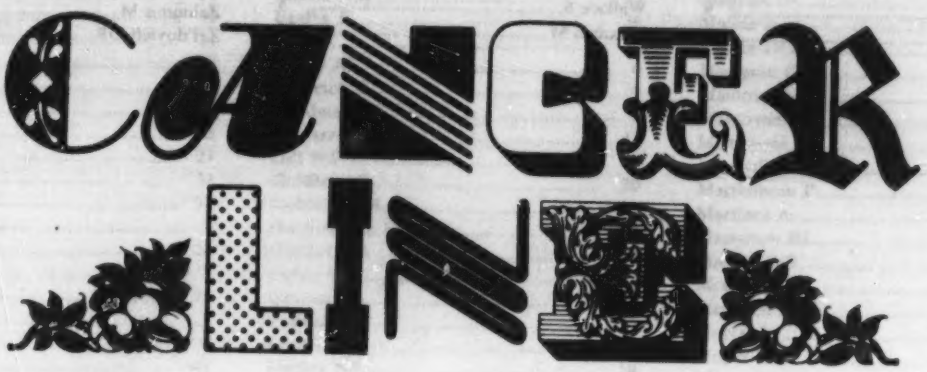

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VULVAR TUMORS

1. CYTOLOGY OF THE EXFOLIATIVE LAYER IN NORMAL AND DISEASED VULVAR SKIN CORRELATION WITH HISTOLOGY.

Nauth HF, Schilke E
Universitats-Frauenklinik, Pilgrimstein 3, D-3550 Marburg 1, W. Germany
Acta Cytol (Baltimore); 26(3):269-283 1982

The vulvae of 464 patients were studied by cytologic and/or histologic examination. Of these, 286 patients had clinically normal vulvae and 178 patients, diseased vulvae. Histology revealed 47 benign, 20 precancerous and 111 malignant lesions. Structural variations of the vulvar stratum corneum could be classified into five categories: orthokeratosis, hyperkeratosis, parakeratosis, dyskeratosis and tumor penetration. Orthokeratosis, hyperkeratosis and parakeratosis were present in the normal vulvae as well as in benign conditions; they were characterized cytologically by anucleated horny squames or by parakeratotic cells. Dyskeratosis usually indicated precancerous or malignant conditions but was also observed, although in mild form only, in certain benign lesions, eg, acute inflammation and condyloma acuminatum. Nevertheless, evidence of dyskeratotic cells in vulvar smears should cause concern because vulvar cancer frequently is covered by a continuous horny (dyskeratotic) layer. Only half of the malignant vulvar lesions showed tumor penetration through this superficial layer, with subsequent exfoliation of tumor cells. (Author abstract) (27 Refs)

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2. INVASIVE CANCER IN THE VULVAR REGION.

Andreasson B, Bock JE, Weberg E
Dept. Obstetrics and Gynecology YA, Rigshospitalet, Blegdamsvej, DK-2100 Copenhagen 0, Denmark
Acta Obstet Gynecol Scand; 61(2):113-119 1982

During the past 25 yr there has been a 10 fold increase in the incidence of vulvar cancer in Denmark. For this reason a material of 195 patients treated during the period 1960-77 is reviewed. There had been a considerable delay in treatment, due partly to the patients and partly to the doctor first seen. The 5-yr survival rate was 63.3%, corrected 84.2%. The prognosis is highly influenced by the size of the tumor, its appearance, the presence of unilateral or bilateral metastasization to the inguinal nodes, the histological type, and localization of the tumor. On the basis of these features, it is possible to single out groups having a particularly poor prognosis in whom the surgical treatment is insufficient and ought to be supplemented. Clinical assessment of the inguinal lymph nodes carries a considerable uncertainly, yet the FIGO staging is based mainly upon this assessment. This goes some way towards explaining why no prognostic differences were found between Stages I, II, and III. Postoperative staging based upon the histological diagnosis would provide greater prognostic certainty. (Author abstract) (17 Refs)

3. CARCINOMA OF THE VULVA: ANALYSIS OF TREATMENT FAILURES.

Podratz KC, Symmonds RE, Taylor WF, Barclay D, Drukker BH, Eichner E
Mayo Clinic, Rochester, MN, 55905
Am J Obstet Gynecol; 143(3):340-351 1982

Continuous follow-up of 224 patients treated for primary invasive squamous cell carcinoma of the vulva in a 20-yr period (1955 to 1975) at the Mayo Clinic resulted in the detection of recurrent (or persistent) neoplasia in 59 (26%). Rates of treatment failure increased with advancing stage of disease - from 14% for Stage I to 71% for Stage IV. The rate of local vulvar recurrence was 18%, which was about three times greater than the recurrence rates for the groin, pelvis, and distant sites. However, the 1-and 5-yr survival rates of 73% and 50%, respectively, after vulvar recurrence were in sharp contrast to the corresponding rates of 34% and 10% for regional or distant recurrence. When 35 patients with central vulvar extension of disease were evaluated, groups at excessive risk for treatment failure (lesions 4 cm or larger or inguinal node involvement, or both) were identified and modifications in conventional therapy applicable to these groups were considered. (Author abstract) (21 Refs)

4. MALIGNANT MELANOMA OF THE VULVA. A REPORT ON 9 CASES.

Charpentier P, Prade M, Bognel C, Gadenne C, Duvillard P
Institut Gustave-Roussy, rue Camille Desmoulins, F 94805 Villejuif Cedex, France
Gynecologie; 32(6):517-522 1981

Malignant melanoma of the vulva was diagnosed in nine women (43-80 yr old). Presenting symptoms included isolated tumor (3 patients), tumor and hemorrhage (2), tumor and pain (1), tumor and itching (1), modification of existing nevus, and modification of an area of melanosis (1). Tumors were located on the small (3 patients) or large (2) lip of the vulva, on the clitoris (2), and on the hemivulva (2). Palpable adenopathy was noted in 2/9 patients. The diagnosis of malignant melanoma was based on histological discovery of the proliferation of atypical melanocytes associated with an excess of melanin, which was accompanied by a junctional activity at the sides of the lesion (5/9 cases). Tumor thickness ranged from 0.79 mm to 15.0 mm. Extension of tumor into fatty tissue was observed only in the two tumors that were 10.0 and 15.0 mm thick. In four patients, lymphatic metastasis was observed (palpable in 2, nonpalpable in 2). Treatment included electrocoagulation, hemivulvectomy, vulvectomy, and tumor excision. Two of the nine patients were alive, one with no sign of recurrence, 13 and 17 yr after treatment. (6 Refs) (In FRE)

CERVICAL AND UTERINE TUMORS

5. THE COMBINED USE OF CYTOLOGY AND COLPOSCOPY IN ENHANCING DIAGNOSTIC ACCURACY IN PRECLINICAL LESIONS OF THE UTERINE CERVIX.

Lozowski MS, Mishriki Y, Talebian F, Solitare G
Dept. Pathology, Nassau Hosp., 259 First St., Mineola, NY, 11501
Acta Cytol (Baltimore); 26(3):285-291 1982

In an attempt to evaluate the accuracy of cytologic and colposcopic findings (alone and in combination) in detecting preclinical lesions of the uterine cervix, diagnosis made in 170 consecutive patients referred for colposcopic examination at Nassau Hospital because of an abnormal Papanicolaou smear were reviewed. We found that of the investigative methods available prior to biopsy, a combined cytologic and colposcopic evaluation is preferred since it is highly accurate in predicting the degree of severity of a lesion (84.6% of all cases reviewed) and, in our experience, eliminates the problem of false negatives, which are encountered when either method is used to the exclusion of the other. (Author abstract) (11 Refs)

6. EXAMINATION OF THE CERVIX WITH THE NAKED EYE USING ACETIC ACID TEST.

Ottaviano M, La Torre P
Via Fabroni 41, Florence, Italy
Am J Obstet Gynecol; 143(2):139-142 1982

Examination of the cervix was carried out on 2,400 patients, by use of acetic acid test with the naked eye and the colposcope. The physiologic transformation zone was clearly identified both with the naked eye and the colposcope in 1,568 of 1,594 (99%) cases. Colposcopic examination was unsatisfactory in 108 of the 264 (41%) patients in whom the cervix was completely covered by normal squamous epithelium. An atypical transformation zone (ATZ) was identified with the naked eye as white epithelium in 98.4% and as 'suspicious' in 1.6% of 312 colposcopically controlled cases. An unsatisfactory colposcopic examination occurred in 39 of the 312 (12.5%) patients with an ATZ. Final histologic diagnosis for 312 ATZs was benign lesion in 169 of 312 (54.2%), cervical intraepithelial neoplasia (CIN) Grades 1 and 2 in 81 of 312 (26%), Grade 3 CIN in 56 of 312 (17.9%), and preclinical invasive carcinoma in 6 of 312 (1.9%). The detection of intraepithelial or preclinical invasive cervical neoplasias should not depend on the possession of a colposcope. On the other hand, the use of a colposcope is essential for the selection of CIN that can be treated with ultraconservative therapy or with colposcopically directed conization. (Author abstract) (8 Refs)

7. ADENOCARCINOMA AND MIXED CARCINOMA OF THE UTERINE CERVIX. I. A CLINICOPATHOLOGIC STUDY.

Fu YS, Reagan JW, Hsiu JG, Storaasli JP, Wentz WB
Inst. Pathology, Case Western Reserve Univ., Cleveland, OH, 44106
Cancer; 49(12):2560-2570 1982

Ninety-two primary glandular neoplasms of the uterine cervix, including 51 endocervical adenocarcinomas, 4 endometroid carcinomas, and 37 mixed carcinomas, were reviewed to define the biologic significance of pathologic features. Pure adenocarcinomas were found to have a better prognosis than mixed carcinomas of comparable stage (overall 5-yr survival rate, 49 vs 36%). Endocervical adenocarcinomas with glandular and papillary patterns had a better prognosis than mucinous adenocarcinomas. When mixed carcinomas were separated into mature, signet-ring, and glassy-cell types, patients with the glassy-cell type had a better 5-yr survival rate than patients with the other two types. However, the long-term prognosis was equally poor. The degree of differentiation as determined by the nuclear features was useful in predicting the outcome in patients with adenocarcinomas. Although the number of cases was small, combined surgery and radiotherapy achieved the best long-term survival for patients with pure adenocarcinomas. This was less apparent for mixed carcinomas. (Author abstract) (32 Refs)

8. CARCINOMA OF THE ENDOMETRIUM. II. PAPILLARY ADENOCARCINOMA: A CLINICAL PATHOLOGICAL STUDY 46 CASES.

Christopherson WM, Alberhasky RC, Connelly PJ
Dept. Pathology, Univ. Louisville, Louisville, KY, 40292
Am J Clin Pathol; 77(5):534-540 1982

Forty-six patients with papillary carcinoma of the endometrium were studied. Forty-five were followed for at least 5 years or until death, and 41 were followed for 10 years. The remaining patient was alive at 4 years. The survival rate was 51.1% at 5 years and 46.3% at 10 years. At 5 years one-third had died of their disease. The median age at time of diagnosis was 63 years, and the age at diagnosis was an important determinant of survival. None of the seven black women survived for 5 years. Tumor grade was an important predictor of the course of disease and nuclear grading was a significantly more accurate indicator than was the histological grading of the World Health Organization. Papillary carcinoma should be distinguished from the papillary type of clear cell carcinoma of the endometrium. While it has a somewhat better prognosis than mixed adenosquamous carcinoma or clear cell carcinoma, it appears to be more aggressive with a lower survival rate and higher rate of death from disease than the usual type of endometrial adenocarcinoma or adenoacanthoma. (Author abstract) (23 Refs)

9. EVALUATION OF CRITERIA FOR DISTINGUISHING ATYPICAL ENDOMETRIAL HYPERPLASIA FROM WELL-DIFFERENTIATED CARCINOMA.

Kurman RJ, Norris HJ
Georgetown Univ. Sch. Medicine, 3800 Reservoir Road, N.W., Washington, DC, 20007
Cancer; 49(12):2547-2559 1982

Endometrial curettings from 204 patients containing severe forms of atypical hyperplasia, carcinoma in situ, and well-differentiated carcinoma were compared with subsequent hysterectomy specimens to evaluate and identify the most useful histologic criteria for predicting the presence of invasive carcinoma. Endometrial stromal invasion, increased degrees of nuclear atypism, mitotic activity, cellular stratification, and epithelial necrosis in curettings were associated with a greater likelihood of carcinoma in the uterus. Of these, stromal invasion was the most significant feature. When stromal invasion was absent, carcinoma was present in the uterus in only 17%, and the carcinomas were well differentiated and confined to the endometrium or only superficially invasive. When stromal invasion was present in curettings, residual carcinoma was present in the uterus in half, and of these, one third were moderately or poorly differentiated and a quarter invaded deeply into the myometrium. The criteria for invasion are (1) an irregular infiltration of glands associated with an altered fibroblastic stroma or desmoplastic response; (2) a confluent glandular pattern in which individual glands are uninterrupted by stroma and merge to form a cribriform pattern of stromal replacement; (3) an extensive papillary pattern; and (4) replacement of stroma by masses of squamous epithelium. To qualify as invasion, items 2, 3, and 4 must occupy at least one half (2.1 mm) a low power field 4.2 mm in diameter. Because of the important role of stromal invasion in predicting prognosis, future classifications of endometrial neoplasia should utilize this feature in distinguishing atypical hyperplasia from well differentiated adenocarcinoma. (Author abstract) (27 Refs)

10. CARCINOMA OF THE ENDOMETRIUM. IV. MIXED ADENOSQUAMOUS CARCINOMA. A CLINICAL-PATHOLOGICAL STUDY OF 68 CASES WITH LONG-TERM FOLLOW-UP.

Alberhasky RC, Connelly PJ, Christopherson WM
(c/o Christopherson) Dept. Pathology, Univ. Louisville, Louisville, KY, 40292
Am J Clin Pathol; 77(6):655-664 1982

In a histologic review of 989 cases of invasive endometrial carcinomas there were 68 mixed adenosquamous carcinomas. Sixty were followed for at least 5 yr, or until death. The other eight were diagnosed in 1976 and were ineligible for 5-yr status evaluation. Twenty-eight of the 60 patients or 46.7% were alive at 5 yr. Twenty-five or 41.7% died of their cancer. Stage of disease, depth of myometrial invasion, vascular invasion, age, and method of treatment all had an impact on end results. By comparison, the absolute 5-yr survival rate for 200 women with adenocanthoma was 87.0%. Thirty patients with atypia of the squamous portion of the adenoacanthoma had an identical survival rate as those without atypia. Combined irradiation and hysterectomy end results were superior to hysterectomy only, or to radiation therapy only. Although one examination of time trends revealed a significant increase in the percentage of all tumors that were diagnosed as adenoacanthoma, there was no increase in the relative frequency of mixed adenosquamous carcinoma. (Author abstract) (25 Refs)

11. ATYPICAL INDIFFERENT (RESERVE) CELLS IN THE CERVICAL EPITHELIUM AND THEIR EXFOLIATIVE PATTERN.

Ruiter DJ, Boon ME
(c/o Boon) Dept. Pathology, S.S.D.Z., Reynier de Graefweg 7, NL-2625 AD Delft, The Netherlands
Acta Cytol (Baltimore); 26(3):292-298 1982

The ultrastructure of light microscopically selected atypical indifferent (reserve) cells in cervical smear preparations is described and compared with their ultrastructure in histologic sections. These atypical indifferent cells have a blastlike chromatin pattern and an intact nuclear membrane. The cytoplasm,

however, was often damaged or absent; if present, it showed no sign of differentiation. In the histologic sections, these atypical indifferent cells were found in reverse-cell hyperplasia, in small numbers in squamoid dysplasia and as basally located cells in atypical endocervical epithelium. In contrast to the indifferent cells, the squamoid dysplastic cells and atypical endocervical cells in smear preparations had intact cytoplasm; however, the nuclear membrane of the squamoid dysplastic cells was often interrupted. This study indicates that atypical indifferent (reserve) cells can be recognized by light microscopy in smear preparations and that the fact that the cytoplasm is often damaged or absent is probably due to its undifferentiated nature. These cells can originate in pure atypical reserve-cell hyperplasia, dysplasia or atypical endocervical epithelium. In view of the great importance of these cells in the morphogenesis of squamoid and adenomatous carcinoma of the cervix, it seems of paramount importance that they be identified in cervical smears. (Author abstract) (17 Refs)

12. GLASSY CELL CARCINOMA OF THE ENDOMETRIUM.

Christopherson WM, Alberhasky RC, Connelly PJ
Dept. Pathology, Univ. Louisville Sch. Medicine, Louisville, KY, 40292
Hum Pathol; 13(5):418-421 1982

A variant of mixed adenosquamous carcinoma of the endometrium was encountered in 5 of 68 patients (7.4%) with mixed adenosquamous carcinomas of the endometrium. A sixth patient had an isolated area of glassy cell carcinoma in an otherwise typical adenosquamous carcinoma. The ground-glass appearance of the cytoplasm, the distinctive nucleus with prominent nucleoli, the numerous mitoses, and the similarity of this tumor to previously described glassy cell cervix cancers all suggest that the tumor is glassy cell carcinoma Four of the five tumors behaved in an aggressive manner. (Author abstract) (7 Refs)

13. URINARY CYCLIC NUCLEOTIDES AND THE CYTOPATHOLOGY OF HUMAN UTERINE CERVICAL DYSPLASIAS.

Duttagupta C, Romney SL, Palan PR, Slagle NS
Dept. Gynecology and Obstetrics, Albert Einstein Coll. Medicine, Ullmann Building, Room 111, 1300 Morris Park Ave., Bronx, NY, 10461
Cancer Res; 42(7):2938-2943 1982

Blinded urinary assays for cyclic guanosine 3':5'-monophosphate (cGMP) and cyclic adenosine 3':5'-monophosphate (cAMP) were performed on 49 subjects with documented abnormal cervical cytology and 21 control subjects with normal cytology. A significant difference in the mean cGMP:cAMP ratios between the case and control groups was found. A significantly greater proportion of women with cytological abnormalities had a cGMP:cAMP ratio above the 0.2 level (p less than 0.001). Cases treated surgically for severe dysplasia or carcinoma in situ of the cervix revealed a significant postsurgical fall in the cGMP:cAMP ratios (p less than 0.025). The possibility of utilizing urinary ratios of cyclic nucleotides as an objective index in the detection, monitoring of progression, and therapy of preneoplastic cervical lesions is discussed. (Author abstract) (27 Refs)

14. ADENOCARCINOMA AND MIXED CARCINOMA OF THE UTERINE CERVIX. II. PROGNOSTIC VALUE OF NUCLEAR DNA ANALYSIS.

Fu YS, Reagan JW, Fu AS, Janiga KE
Inst. Pathology, Case Western Reserve Univ., Cleveland, OH, 44106
Cancer; 49(12):2571-2577 1982

The prognosis of the glandular neoplasms of the uterine cervix is related to the clinical stage and, to a lesser extent, to the histologic type, growth pattern, and degree of differentiation of the neoplasms. To determine further the prognostic significance of the stem cell ploidy levels as determined by nuclear DNA quantitation, the authors separated the tumors into low ploidy (less than 3N) and high ploidy (greater than 3N) groups. Of the clinical Stage I and II neoplasms, low ploidy tumors had a better prognosis than high ploidy tumors of comparable stage. Low ploidy tumors had a better prognosis than high ploidy tumors irrespective of the degree of differentiation. Mixed carcinomas had a poorer prognosis than pure adenocarcinomas of comparable clinical stage. This might be explained by the greater proportion of high ploidy stem cells in mixed carcinomas than in pure adenocarcinomas. Although advanced clinical Stage III and IV neoplasms had a poor outlook regardless of the DNA ploidy level, there was a proportional increase of high ploidy tumors with increasing clinical stage. These findings suggest that cervical glandular neoplasms having high ploidy stem cell lines are biologically more aggressive than those with low ploidy stem cell lines. (Author abstract) (9 Refs)

15. LEIOMYOMAS: STEROID RECEPTOR CONTENT. VARIATION WITHIN NORMAL MENSTRUAL CYCLES.

Soules MR, McCarty KS
Duke Univ. Medical Center, Box 3711, Durham, NC, 27710
Am J Obstet Gynecol; 143(1):6-11 1982

In an attempt to clarify further the relationship between ovarian function and uterine leiomyomas, we investigated the cytoplasmic estrogen and progesterone receptor content in these uterine tumors. The study population consisted of 17 women of reproductive age at various stages of ovulatory menstrual cycles. Serum samples were analyzed for estrogen and progesterone content; tissue samples from endometrium, myometrium, and leiomyomas were analyzed for cytoplasmic estrogen and progesterone receptor content. The levels of cytoplasmic estrogen and progesterone receptor in leiomyomas demonstrated the same quantitative and qualitative cyclic changes throughout the menstrual cycle apparently in response to variations in circulating estrogen and progesterone as found in endometrium and myometrium. (Author abstract) (16 Refs)

16. IS CONIZATION APPROPRIATE TREATMENT FOR CERVICAL CANCER IN SITU?

Lambert B, Rousseau S, Bielmann P, Lamoureux E, Boivin Y
Departement d'obstetrique et gynecologie, Hotel-Dieu de Montreal, 3840 rue St-Urban, Montreal PQ H2W 1T8, Canada
Can Med Assoc J; 126(10):1176-1177 1982

Effectiveness of conization (CN) as a treatment for cervical cancer in situ was studied reviewing charts of 111 patients (16-66 yr old, mean age 38.8 yr) who had undergone CN. Patients were divided into Group A, 71 women who desired sterilization and underwent hysterectomy after CN, and Group B, 40 women who underwent CN only. Among the Group A patients the cone was complete in 22 and incomplete in 43. Hysterectomy was significantly less likely to reveal uterine in-

volvement in the patients whose cones were complete than in those whose cones were incomplete. Excluding 6 patients who had vaginal involvement, 32 patients were cured by CN. Group B patients were ineligible for cryosurgery. Seventeen Group B patients whose cones were incomplete were significantly younger than patients whose cones were complete (24.4 vs 28.5 yr). Pathological studies showed that in 80% of patients the lesions were large-cell, nonkeratinized, moderately differentiated Grade 2 cancers; the rest of the lesions were large-cell keratinized cancers. In Group A endocervical involvement was found in 37 of 43 patients whose cones were incomplete and in 5 of 22 whose cones were complete, but in Group B only 1 patient in each subgroup showed longitudinal extension of the disease. Among patients whose cones were incomplete, circumferential involvement was more pronounced in Group B (four-quadrant invasion), than in Group A (three-quadrant invasion). Overall, no particular quadrant was involved more than the others. Neither age nor parity was significantly related to cone size. (20 Refs)

17. WHAT IS THE OPTIMUM TREATMENT OF CERVICAL PREMALIGNANCY?

Singer A, Walker P
Dept. Gynaecology, Whittington Hosp., London, England
Br J Obstet Gynaecol; 89(5):335-337 1982

Optimum treatment and cryotherapy of cervical premalignancy is reviewed. Cryotherapy has probably a greater role in the treatment of cervical intraepithelial neoplasia (CIN) I and II lesions (mild, moderate dysplasia); controversy surrounds the actual premalignant potential of these abnormalities but it seems certain that CIN II should be eradicated. Electrodiathermy coagulation is a slightly more destructive technique and the same criteria have to be applied. At least three-quarters of young women with CIN III lesion are suitable for one or other of the locally destructive procedures provided that strict colposcopic and histological criteria outlined are adhered to. (16 Refs)

18. A NEW ENDOMETRIAL APPLICATOR.

Nori D, Hilaris B, Anderson L, Lewis JL
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Int J Radiat Oncol Biol Phys; 8(5):941-945 1982

An afterloading applicator for the treatment of cancer of the endometrium was designed to maintain the afterloading system which has been in continuous use as part of intracavitary and interstitial techniques. The insertion and removal of the applicator was simplified causing very little injury to the cervix and the corpus of the uterus; furthermore, it permits a one-step irradiation of both uterus and vagina. The technique of intracavitary application is described. (2 Refs)

19. INTRAOPERATIVE RADIATION IN THE TREATMENT OF ADVANCED CERVICAL CARCINOMA (MEETING ABSTRACT)

Delgado G, Bodle A, Hill L, Goldson A, Petrilli E
Georgetown University Hospital, Washington, DC
Am J Clin Oncol; 5(2):139 1982

Fifteen patients with advanced cervical carcinoma were treated with intraoperative radiation using electron beam. Ten patients presented with positive paraaortic nodes, two with negative nodes, and three with recurrent disease localized in the pelvis after treatment with conventional x-ray therapy. All patients had an exploratory laparotomy with selective paraaortic and pelvic lymphadenectomies. Twelve patients with primary disease received doses of 1000-2500 rad to the paraaortic nodes. In addition, the patients with primary disease were treated postoperatively by external beam radiation to the pelvis followed by intercavitary applications. Patients with recurrent disease received 2000-3000 rad to the pelvic wall and/or tumor areas. In the group with positive paraaortic nodes, 20% are alive and clinically free of disease at 6 and 9 months. One of the patients with biopsy-proved positive paraaortic nodes at the time of primary surgery underwent a reexploration 7 months after intraoperative radiation, and at the time the lymph glands were negative for metastatic disease. Both patients with negative paraaortic nodes were free of disease at 12 and 24 months. In the group treated for recurrent disease, all patients (3) had relief of their symptoms following intraoperative radiation. One patient has remained free of disease for 8 months. Two of the 15 patients developed significant complications: persistent intractable pain with motor weakness directly related to the femoral nerve. Both of these patients are free of disease. This complication has been avoided by placing a lead shield over the top of the psoas muscle. (no Refs)

20. ANALYSIS OF COMPLICATIONS AFTER IRRADIATION OF CARCINOMA OF THE UTERINE CERVIX (MEETING ABSTRACT)

Perez CA, Madoc-Jones H, Bedwinek JM, Purdy JA, Breaux S, Powers WE
Washington University School of Medicine, St. Louis, MO
Am J Clin Oncol; 5(2):135 1982

A total of 813 patients with invasive carcinoma of the uterine cervix were treated with radiation therapy alone between 1959 and 1977. All patients are available for a minimum of 3 years' follow-up. Patients were staged according to the FIGO classification. Radiation therapy consisted of a combination of external irradiation to the whole pelvis (1000-2000 rad) and parametria (for a total of 4000-5000 rad) and two intracavitary radioactive source insertions (6500-7500 mgh). Patients with Stages IIB, III, and IVA have been consistently treated with somewhat higher doses of external irradiation and intracavitary insertions. An additional group of 63 patients had pelvic lymphadenectomy following the irradiation. The records and dosimetry of these patients have been carefully reviewed. Doses of irradiation to the lateral portion of the cervix, paracervical tissues, bladder, and rectum have been recalculated in 60% of the patients using the actual implant films and isodose curves and with reconstructions of the intracavitary insertions in the remaining 40%. The current study analyzes the significance of a variety of technical factors on the incidence and severity of treatment complications, such as total dose to specific organs, portion of external whole-pelvis irradiation, intracavitary doses, number of applications, position of the applicators, etc. A dose-response curve for various clinical stages has been constructed correlating the dose to the bladder or the rectum with the incidence of major complications. (no Refs)

21. RESIDUAL CARCINOMA AFTER INTRACAVITARY IRRADIATION OF ENDOMETRIAL CARCINOMA, STAGE I. A STUDY OF WHOLE-ORGAN SECTIONS.

Grontoft O, Risberg B, Stenson S, Westholm B
Dept. Pathology I, Univ. Hosp., S-581 85 Linkoping, Sweden
Acta Obstet Gynecol Scand; 61(2):163-172 1982

Surgical specimens from 87 patients with endometrial carcinoma, Stage I, preoperatively treated by intracavitary irradiation were investigated by a whole-organ sectioning technique.

Re-examination of the curettage material showed cancer Stage 0 in 8 (9%) and carcinoma Stage I in 79 cases (91%). In the Stage I cases 57% showed residual carcinoma localized mainly to the myometrium of the uterine body and cornuae. Histological changes in the carcinoma were unevenly distributed, but tumors growing close to the external uterine surface were well preserved. In 40.5%, no carcinoma was present, and in 2.5% the changes found could not be classified. Correlated to disparity in irradiation technique, no significant difference could be demonstrated in the incidence or localization of residual carcinoma. The most important single pretreatment factor combined with the presence of residual carcinoma was myometrial fragments with infiltrating carcinoma in the curettage material (MICC). Computerized analysis of combinations of factors showed that all patients aged over 60 yr with a uterine-sound length exceeding 8 cm had residual carcinoma. Only two patients with infiltration of the myometrium had a completely destroyed carcinoma. The findings indicate that it is unlikely that endometrial carcinoma Stage I with myometrial invasion will be eradicated by intracavitary irradiation. (Author abstract) (26 Refs)

22. CALIFORNIUM-252 NEUTRON CURIETHERAPY FOR ADVANCED CERVICAL CANCER.

Maruyama Y, Bell PR, Yoneda J, Van Nagell JR
Dept. Radiation Medicine, Univ. Kentucky Medical Center, Lexington, KY, 40536
Oncology; 39(4):209-215 1982

Low dose rate neutron radiotherapy using fast neutrons emitted by the radionuclide 252Cf was combined with fractionated x- or gamma rays for the radiotherapy of advanced cervicovaginal tumors. Two different implants schedules were tested to determine the response of the tumors to the scheduling of therapy with the 252Cf either early or delayed in the fractionated radiotherapy course. A 90% frequency of complete local clearance of pelvic tumors was observed by the early application of 252Cf. Neutron curietherapy applied as a boost treatment at the end of fractionated radiotherapy, resulted in only 40% local control. Improved results were observed by early implantation therapy and is postulated to be the result of more effective hypoxic tumor therapy and reoxygenation of the hypoxic pelvic tumor. The two groups of patients were compared as to their general status and medical condition and were found similar in age, frequency of associated disease, body weight and tumor stage. The failures of local control by early 252Cf neutron therapy, occurred in two patients with high-stage tumor and severe vascular disease and suggests that tumor response was partly dependent upon the integrity and elasticity of the small vessel system. (Author abstract) (33 Refs)

23. TREATMENT OF ENDOMETRIAL CARCINOMA WITH RADIATION THERAPY ALONE.

Abayomi O, Tak W, Emami B, Anderson B
Tufts-New England Medical Center, 171 Harrison Ave., Boston, MA, 02111
Cancer; 49(12):2466-2469 1982

Of 393 patients treated at Tufts-New England Medical Center for endometrial carcinoma from 1968-1977, 66 patients underwent radiation therapy alone because of medical contraindications to surgery. The median age for this group was 70 yr. The patient distribution was Stage I (39), Stage II (11), and Stage III and IV (16). Therapy consisted of pelvic irradiation to a dose of 4,000-5,000 rad followed by an intrauterine radium application (3,000-5,000 mg hr) and a vaginal radium application (2,000-4,000 rads to the surface). Local control was achieved in 37 of 50 patients with Stages I and II disease with a 3-yr actuarial survival of 78%. Patients with Stages III and IV disease had a median survival of 15 mo; 4 of 16 patients survived for 36 mo. In this group of patients, bleeding, pain, and vaginal discharge was palliated. Four patients in the series had treatment-related bowel complications requiring colostomy. This is an effective method of treatment for endometrial carcinoma patients who are not surgical candidates. (Author abstract) (10 Refs)

24. INFLUENCE OF PRIOR ABDOMINAL/PELVIC SURGERY ON THE COMPLICATION RATE OF PATIENTS TREATED WITH RADIATION THERAPY FOR CANCER OF THE UTERINE CERVIX (MEETING ABSTRACT)

Davis ML, Orr JW, Shingleton HM, Levy DS, Brascho DJ
Department of Radiation Oncology and Division of Gynecology Oncology, University of Alabama in Birmingham, Birmingham, AL, 35294
Am J Clin Oncol; 5(2):136 1982

Radiation oncologists are acutely aware of the mobidity associated with radiation therapy for cancer of the cervix. Recently, there has been growing concern that the increased frequency of surgical staging of these patients may be a major contributing factor in the development of intestinal and urogenital complications encountered after radiation therapy. We have recently analyzed the incidence of major complications developed by 624 cervical carcinoma patients treated with radiation therapy during the period 1967 to present. Major complications were classified as: fistulas-all types; bowel-adhesions, strictures, obstructions, or perforations; ureteral-stenosis or obstruction; and bladder-strictures, adhesions, or hemorrhagic cystitis. Of the 624 patients in this study, 117 (18.8%) underwent surgical staging procedures, 120 (19.2%) had received some type of abdominal/pelvic surgery more than 6 months prior to radiation therapy, and 387 (62.0%) had a negative history of abdominal or pelvic surgery at the time of their radiation therapy. Within 3 months to 3 years following radiation therapy, 29 (24.8%) of the 117 surgically staged patients, 18 (15%) of the 120 prior surgery (not surgically staged) patients, and 36 (9.3%) of the 387 non-prior surgery patients developed one or more of the major complications described above. (no Refs)

25. TREATMENT OF MICRO-INVASIVE EPITHELIOMA OF THE CERVIX UTERI.

Castaigne D, Michel G, George M, Prade M
Service de Chirurgie, Institut Gustave-Roussy, rue Camille-Desmoulins, F 94800 Villejuif, France
Gynecologie; 32(6):533-537 1981

Treatment of 24 patients (22-60 yr old) with microinvasive cervical carcinomas, who presented with metrorrhagia (6 patients), other diverse gynecological disorders, or who were asymptomatic (12), is described. Clinical examination was normal in 20% of the patients and pathologic in 80%. Of the 24 cases of microinvasive carcinomas, 2 were diagnosed preoperatively as intraepithelial carcinoma or as carcinoma in situ, 4 were not definitively diagnosed, and in 6 cases the junctional zone was not located by colposcopy. Treatment included colpohysterectomy (5 patients), hysterectomy (10), intravaginal amputation of the cervix (8), and cervicectomy (1). Fifteen of the 24 patients received no adjuvant therapy. Six other patients received vaginal curietherapy when histological examination of the revealed tumor cells at the edge of the vaginal resection. One patient had vaginal curietherapy 1 yr after hysterectomy

for a vaginal recurrence (intraepithelial carcinoma). All 24 patients were cured, 4 with greater than 4 yr follow-up. Current treatment of microinvasive cervical carcinomas is discussed. (8 Refs) (In FRE)

26. BLEOMYCIN AND MITOMYCIN-C (BLM-M) IN RECURRENT SQUAMOUS UTERINE CERVICAL CARCINOMA.

Boice CR, Freedman RS, Herson J, Wharton JT, Rutledge FN
(c/o Freedman) Dept. Gynecology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Texas Medical Center, Houston, TX, 77030
Cancer; 49(11):2242-2245 1982

Bleomycin and mitomycin-C (BLM-M) induction therapy was administered to 23 patients with recurrent squamous carcinoma of the uterine cervix. Six patients (26%) responded. Although these results are much lower than originally reported with BLM-M, there is statistical evidence that patients with disease outside the previous radiation therapy field have improved or more easily determined responses. There was no difference in survival between responders and nonresponders for patients who survived at least 6 wk. Therapy was found to be relatively nontoxic with no deaths related to therapy. (Author abstract) (8 Refs)

27. FOUR-DRUG COMBINATION CHEMOTHERAPY FOR ADVANCED CERVICAL CARCINOMA.

Chan WK, Aroney RS, Levi JA, Tattersall MH, Fox RM, Woods RL
(c/o Levi) Oncology Dept., Royal North Shore Hosp., St. Leonards, N.S.W. 2065, Australia
Cancer; 49(12):2437-2440 1982

Thirty-one patients with advanced stage squamous carcinoma of the cervix were treated with the four-drug combination fluorouracil, doxorubicin, cyclophosphamide, and vincristine. Four patients achieved complete remission (13%) and 15 partial remission (45%). The only factor of adverse prognostic significance was poor initial patient performance. Median survival for the patients entering complete remission exceeded 54 wk and was 43 wk for patients achieving partial remission. Seven patients are still alive at 50 wk. This represents a notable prolongation of survival compared with those patients who did not achieve remission. Toxicity for the combination was not excessive; myelosuppression and vincristine-induced neuropathy were the most prominent. These results are moderately encouraging and confirm the sensitivity of cervical carcinoma to systemic chemotherapy. Further studies to define the optimal use of chemotherapy in both advanced and earlier stages of disease are warranted. (Author abstract) (17 Refs)

28. COMBINATION CHEMOTHERAPY FOR ADVANCED ENDOMETRIAL CANCER. AN EVALUATION OF THREE REGIMENS.

Horton J, Elson P, Gordon P, Hahn R, Creech R
Div. Oncology, Albany Medical Coll., Albany, NY, 12208
Cancer; 49(12):2441-2445 1982

In patients with advanced uterine corpus carcinoma treated with the combination chemotherapy of megestrol, cyclophosphamide, and doxorubicin (MCA) or with this combination and 5-fluorouracil (MCAF), the overall response rate was 22%. There was no significant difference in response rates between the two regimens. There is some indication that survival was longer in ambulatory patients who were treated with MCA, but this combination produced more hematologic toxicity than MCAF. Patients unsuitable for treatment with doxorubicin received megestrol, 1-phenylalanine mustard, and 5-fluorouracil (MLF), which produced objective responses in 2 of 12 patients. (Author abstract) (9 Refs)

29. IMMUNOSTIMULATION WITH VITAMIN A IN ADVANCED CERVICAL CARCINOMA.

Kucera H, Micksche M
I. Univ.-Frauenklinik, Spitalgasse 23, A-1090 Wien, Austria
Fortschr Med; 100(16):760-763 1982

Treatment of advanced, inoperable cervical carcinoma with vitamin A palmitate (VAP) and radiotherapy (RT) was studied. Twenty-one women received VAP and RT; 21 received only RT. In response to phytohemagglutinin increased blastogenic response was found in 66% of those receiving VAP and RT and 33% of those receiving only RT. VAP evidently affects T-cell response. Patients receiving VAP had an insignificantly lower rate of relapse than those receiving only RT. Further studies of VAP are warranted. (20 Refs) (In GER)

30. PROGRESSION TO MALIGNANCY OF SEVERE DYSPLASIA OF THE UTERINE CERVIX.

Yajima A, Sato A, Mori T, Wakisaka T, Sato S, Suzuki M, Teshima K, Noda K
Dept. Obstetrics and Gynecology, Tohoku Univ. Sch. Medicine, Sendai 980, Japan
Tohoku J Exp Med; 136(4):433-438 1982

The site within the cervix of dysplasia and carcinoma in situ and follow-up results of 654 patients with severe dysplasia and 691 with mild dysplasia are discussed. Particular emphasis is placed upon the correlation of these parameters with histological maturity of dysplastic lesions. Only two cases (0.3%) of the mild dysplasia cases showed carcinoma in situ at follow-up. In contrast, 80/654 (12.2%) cases of severe dysplasia showed carcinoma in situ and 31/654 showed microinvasive carcinoma. Histological evaluation revealed 204 cases of immature type, 245 of premature type, and 205 of mature type. The rate of progression to malignancy was nearly 5x higher in cases of immature type dysplasia than in mature type. It was found that 58/111 cases which progressed to malignancy were of the immature type, 41/111 were of the premature type, and 12/111 of the mature type. In the cases of carcinoma in situ progressing from immature dysplasia, the majority were of the small cell type, whereas in cases progressing from mature dysplasia, most were of the large cell type. Forty percent of the microinvasive cases progressing from immature dysplasia were of the small cell non-keratinizing type and 53.3% were of the large cell non-keratinizing type, while 80% of such cases progressing from mature dysplasia were of the keratinizing type. Patterns of location of these three lesions were similar. Locations of immature dysplasia lesions were found to be similar to those of the S-type carcinoma in situ lesions. (5 Refs)

31. SEX PARTNERS AND HERPES SIMPLEX VIRUS TYPE 2 IN THE EPIDEMIOLOGY OF CANCER OF THE CERVIX.

Graham S, Rawls W, Swanson M, McCurtis J
Dept. Social and Preventive Medicine, State Univ. New York at Buffalo, 2211 Main St., Buffalo, NY, 14214
Am J Epidemiol; 115(5):729-735 1982

The authors examined the interaction of exposure to various numbers of sex partners and evidence of antibodies to herpes simplex virus type 2 (HSV-2) in cervical neoplasia in 181 cases of cervical dysplasia, carcinoma in situ and cancer of the

cervix and 130 control patients in Los Angeles County, California hospitals, in 1974-1979. Studies by the authors and other investigators have found that risk of cancer of the cervix was enhanced with numbers of sex partners, frequency and duration of using the vaginal douche, early age at first pregnancy, and antibodies to HSV-2 as measured by radioimmunoassay. In this study, it was found that for women with only one or no sex partner in their history, risk was elevated if evidence of antibodies to HSV-2 were present. The same was true for women with two or more sex partners. The risk associated with two or more sex partners was not higher than that for women with one sex partner among those positive for HSV-2, and among those negative for HSV-2. Thus, although this inquiry needs replication on larger numbers of women, whatever the other microorganisms of carcinogens patients were exposed to with multiple sex partners, there was no apparent effect beyond the fact the HSV-2 raises the risk of cancer of the cervix. This may strengthen credence in the hypotheais that HSV-2 is an etiologic factor in cervical cancer. (Author abstract) (12 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

32. OVARIAN SCLEROSING STROMAL TUMORS: CLINICOPATHOLOGIC STUDY OF 10 CASES.

Tang MY, Liu TH
Dept. Gynecology and Obstetrics, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Chin Med J [Engl]; 95(3):186-190 1982

The clinical features of 10 cases of ovarian sclerosing stromal tumors are reviewed. The age range was 17-59 yr, averaging 35.7 yr. Clinical courses varied between 6 mo to 5 yr. The majority (70%) of the cases were from young women (17-32 yr old). Major symptoms were menstrual disorders manifested as menorrhagia, prolongation of the menstrual period, shortening of the menstrual cycle and irregular menstruation. Both menstrual disorders and problems of infertility were corrected in most cases following tumor excision. This verifies the fact that ovarian sclerosing stromal tumors have some definite endocrine activities, displayed as a high estrogen level and a disturbance in reproductive activity. pathological examination shows that the tumor has both gross and microscopic features of ovarian fibroma, thecoma, and lipoid cell tumor. The tumor is a mixture of fibromatous and lipoid cells separated by edematous or sclerosing stroma into nodules or pseudonodules, together with abundant thin-walled vessels. The tumor cells are mucicarmine and PAS negative and fat stain positive. Single and small clusters of tumor cells are surrounded by reticular fibers. Sclerosing stromal tumors apparently arise from ovarian stroma. Most ovarian sclerosing stromal tumors are clinically and morphologically benign. (4 Refs)

33. OVARIAN TUMOURS OF WOLFFIAN OR ALLIED NATURE: THEIR PLACE IN OVARIAN ONCOLOGY.

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Dept. Morbid Anatomy, Sch. Medicine, Univ. Coll. London, Univ. St., London WC1E 6JJ, England
J Clin Pathol; 35(5):526-535 1982

Two unusual ovarian tumors thought to be of Wolffian identity, one of them malignant, are described. They showed packed combinations of adenopapillary, tubular, trabecular and diffuse patterns, a sharp and generalized periodic acid-Schiff (PAS)-positive basement membrane and areas of elastic network. A review of published Wolffian tumors at various sites suggests that the prototypes of the two tumors occur chiefly in the cervix and broad ligament. The significance of Wolffian tumors and their differentiation from arrhenoblastoma and serous tumors is discussed. (Author abstract) (62 Refs)

34. THE USE OF CYSTINE AMINOPEPTIDASE TO MONITOR OVARIAN CANCER (MEETING ABSTRACT)

Morgan LR, Priebe CJ, Gillen LE, Krupp PJ, Weatherall TJ
Department of Pharmacology, Louisiana State University Medical Center, New Orleans, LA
Med Pediatr Oncol; 10(1):98 1982

Serum cystine aminopeptidase (CAP) activities have been reported to be elevated in patients with ovarian cancer. The present study attempts to correlate stage of disease, response to Adriamycin-Platinol therapy, age and serum CAP activities. In the present study, 22 female patients, age 26-81 with stage II-IV ovarian cancer were evaluated. Thirty healthy non-pregnant females of similar ages, served as control. All patients with cancer had serum CAP activities greater than 6 OD units. One patient with stage II disease had a value of 8 and all other patients had values 11 or greater. The greater the extent of the disease, the larger the values. All patients received therapy with Adriamycin -50 mg/m2 and Platinol -70 mg/m2 every three weeks. Twelve objective remissions (Complete and partial remissions, 3 CR and 9 PR) with 3 stabilizations of disease (SD) and 7 with increasing disease (ID) were observed. All responses were for a minimum of 3 months. One patient with a CR developed a normal value for CAP activities. Two other patients despite no detectable disease (CR), had CAP activities of 13 and 16, respectively. All PR's had elevated CAP values. All patients that responded to chemotherapy had a dramatic reduction in serum CAP activities. For those patients achieving a CR or PR and asymptomatic, no other laboratory values were abnormal despite the elevated CAP for all but on CR. CAP appears to be a useful enzyme to follow response to therapy and disease status in ovarian cancer. (no Refs)

35. PERIPHERAL VENOUS CONCENTRATIONS OF OESTROGENS IN POSTMENOPAUSAL WOMEN WITH OVARIAN CANCER.

Heinonen PK, Tulmala R, Pyykko K, Pystynen P
Dept. Obstetrics and Gynecology, Univ. Central Hosp., Tampere, Finland
Br J Obstet Gynaecol; 89(1):84-86 1982

Serum concentrations of estrone, estradiol and estriol were measured in 23 postmenopausal women, 12 with ovarian cancer and 11 with genital prolapse. Estrone (387.6 pmol/l) and estradiol (72.7 pmol/l) levels were higher in the cancer group than those in the control group (159.8 and 27.5 pmol/l respectively), while estriol levels did not differ (434.5-270.8 pmol/l). The results indicate abnormal ovarian function in postmenopausal patients with ovarian cancer. (Author abstract) (11 Refs)

36. MONONUCLEAR-CELL INFILTRATION IN OVARIAN CANCER. I. INFLAMMATORY-CELL INFILTRATES FROM TUMOUR AND ASCITES MATERIAL.

Haskill S, Becker S, Fowler W, Walton L
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Cancer; 45(5):728-736 1982

Malignant effusions and tumor tissue obtained at surgery provided material for a study of the prognostic value of the various inflammatory cells in the prognosis of human ovarian cancer. Ascitic fluids predominantly contained inflammatory cells; tumor cells, both singly and in clusters, were a minor component. Tumor cells were usually in excess in dispersed solid material. Some patients had significant proportions of lymphocytes and macrophages in their solid tumor, and these patients invariably responded to therapy. Sedimentation-velocity separation at unit gravity provided two populations of inflammatory cells. One consisted of mononuclear cells similar in size to those in the patients blood: the other consisted of one or more large macrophage populations, distinct in morphology and enzymatic markers from both blood monocytes and each other. T lymphocytes were enriched in ascites fractions (78%) and in the tumor-derived mononuclear fraction (71%) compared to patient blood (60%). The T-cell subset characterized by ANAE reactivity was markedly depleted in the tumor-infiltrating fraction (17%) relative to either the ascites (62%) or patient blood (51%). Esterase-positive monocyte-like cells were more frequent in the tumor-infiltrating fraction (17%) than in ascites (7%) or blood (12%). B lymphocytes were infrequent in solid tumors and difficult to assess in ascites. Histiocyte-like macrophages were present in the higher-velocity tumor-cell containing fractions of both solid and ascitic material. The variation in infiltrating cells between patients and between tumor and ascites of the same individual was marked. (Author abstract) (29 Refs)

37. MONONUCLEAR-CELL INFILTRATION IN OVARIAN CANCER. II. IMMUNE FUNCTION OF TUMOUR AND ASCITES-DERIVED INFLAMMATORY CELLS.

Haskill S, Koren H, Becker S, Fowler W, Walton L
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Cancer; 45(5):737-746 1982

Mononuclear cell fractions were isolated from blood, ascites and solid tumors of patients undergoing surgery for Stages III and IV adenocarcinoma of the ovary, and evaluated for their response in NK, ADCC and PHA assays. Control experiments with the same fraction of normal blood indicated that these responses were not influenced by the enzymes used to isolate the tumor and ascites inflammatory cells. The inflammatory cell fractions isolated from both tumor sites which sedimented in the velocity range of blood mononuclear cells were adequate in number and composition for comparison with similar cells from blood. E RFC values in both ascites and tumor fractions exceeded those of patient blood. However, there was a marked difference in distribution of the T subsets between blood, ascites and tumor, which could cause the variable test results between the different cell sources. PHA responses of patient blood and ascites fractions were about half that of normal blood. Tumor-infiltrating lymphocytes (TIL) were less than 10% as responsive as normal blood. The depressed PHA responses of the TIL were not due to the presence of a suppressor cell population. NK activity of patient blood was less than that of normal blood, but not as much as the ascites or TIL cells. The activity of the ascites-derived lymphocytes was enhanced by treatment with interferon. ADCC activity against both CRBC and SB cells was normal or higher than controls in patient blood, and depressed in the ascites-derived fractions. TIL responded to less than 10% of the patient blood values. The results indicate a lack of response by ascitic and TIL cells in assays dependent on FcR-bearing effector cells and a greater loss of PHA-reactive cells from the tumor than from blood and ascites. These data could result from intratumor inactivation, or a failure of the particular subset to localize either in the ascites or the tumor site. (Author abstract) (32 Refs)

38. MONONUCLEAR-CELL INFILTRATION IN OVARIAN CANCER. III. SUPPRESSOR-CELL AND ADCC ACTIVITY OF MACROPHAGES FROM ASCITIC AND SOLID OVARIAN TUMOURS.

Haskill S, Koren H, Becker S, Fowler W, Walton L
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Cancer; 45(5):747-753 1982

Macrophages have been isolated from ascitic and collagenase-dispersed tumors from patients undergoing surgery for ovarian cancer. Macrophages were present in varying proportions in both sites, though the ratio of macrophages to tumor cells was higher in ascites. Marked variation in size (as detected by sedimentation velocity) and cytochemical markers in the macrophages was noted. Highly enriched macrophage fractions were isolated from the ascites and collagenase-dispersed solid tumors by a combination of sedimentation velocity and selective EA RFC or adherence techniques. Suppressor activity in the PHA assay was detected in tumor macrophages (4/10 giveing greater than 50% inhibition), ascitic macrophages (1/15) and blood monocytes (2/7). Lymphocyte fractions from tumors were unresponsive to PHA and failed to suppress the blood response. Suppressor activity was also present in the purified tumor-cell fraction of 6/14 patients. ADCC activity was tested in a few patients. When the activity was determined against the SB target cells, tumor-derived macrophages were inactive, whereas the ascitic fraction showed low but significant activity which averaged much lower than patient blood values. The ADCC assays carried out with the CRC target cell indicated activity within the range of patient blood values in 4/4 ascites and 2/4 tumor macrophage fractions. Cytotoxicity was also assessed against co-purified autologous tumor cells. Although activity was detected in many of the tests, the results seemed to reflect target cell sensitivity. There appeared to be a correlation between cytotoxicity with test macrophages and normal blood mononuclear cells. The results indicate that the cytochemical heterogeneity and the variation in size between macrophage fractions is associated with a spectrum of activities. (Author abstract) (24 Refs)

39. LEVELS OF CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH OVARIAN CANCER.

Clarke AG, Vasey DP, Symonds EM, Farahian B, McLaughlin PJ, Price MR, Baldwin RW
Dept. Obstetrics and Gynecology, Univ. Hosp., Queen's Medical Centre, Nottingham NG7 2UH, England
Br J Obstet Gynaecol; 89(3):231-237 1982

Sera from patients with ovarian tumors were assayed for circulating immune complexes (CIC) by four well established assays based on the interaction of immune complexes with components of the complement system. There was no difference in control, pre- or post-operative or BCG-treated patients' sera. Levels were also unchanged in sera in antigen excess. In patients with ovarian tumors before the measurement of CIC

would appear to be of little value as a screening test, as a guide to the extent of disease, prognosis or therapy. In a small pilot therapy-trial there was no difference in the survival rate between patients with Stage III and IV ovarian cancer treated with cyclophosphamide plus BCG and those who received only cyclophosphamide. Treatment with BCG was associated with postoperative pyrexia and a prolonged hospital stay. (Author abstract) (43 Refs)

40. DEBULKING SURGERY AND SECOND LOOK OPERATION.

Averette HE, Sevin BU
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. Miami Sch. Medicine, Miami, FL
Int J Radiat Oncol Biol Phys; 8(5):891-892 1982

Primary surgery and second-look operation of Stage III and IV ovarian cancer are discussed. Ovarian staging is done surgically. An important aspect of exploration is the exact description of tumor burden and localization. Once the abdominal cavity has been explored, the resectability of the existing tumor masses has to be determined. An omentectomy should be part of every surgical procedure for ovarian cancer for diagnostic and for therapeutic reasons. An appendectomy should also be part of the debulking procedure for ovarian cancer malignancy because of frequent tumor involvement. Primary indication of 'surgical reassessment procedure' is re-operation after a full course of treatment including surgery and chemotherapy for 12-18 mo in asymptomatic patients without any clinical evidence of disease. Once a patient has been explored surgically but optimal tumor resection had not been achieved as part of the primary therapeutic effort, or the tumor had regrown to a sizable mass during chemotherapy, a re-exploration with a second debulking procedure may be indicated before the second mode of chemotherapy is employed. Some reports have proposed laparoscopy as a second-look procedure which may be of value if persistent disease is evident on inspection. Laparoscopy after extensive primary surgery followed by chemotherapy or radiation therapy is associated with a high complication rate, especially bowel injury. (5 Refs)

41. CHEMOTHERAPY IN ADVANCED DISEASE.

Young RC, Myers CE, Ozols RF, Hogan WM
Medicine Branch, NCI, NIH, Bethesda, MD
Int J Radiat Oncol Biol Phys; 8(5):899-902 1982

Role of chemotherapy in advanced ovarian carcinoma (Stages III and IV) is reviewed. Single alkylating agent chemotherapy has been used for patients with bulky residual disease. Response rates of 33-65% can be anticipated with this form of therapy. Median survivals for all treated patients range from 10-14 mo with median survivals of 17-22 mo in those responding to treatment. A summary of some of the active single agents is provided. Several combination chemotherapy studies appear to significantly increase response rates over those achieved with single agents. Combination chemotherapy has produced overall response rates which vary from 22-91% with complete remission rates of 10-69%. A summary of some of the most important combinations are listed. Although the reports are encouraging, it is apparent that the improved results obtained with combination in comparison to single agents are most significant for patients with minimal residual disease. In a prospective trial comparing L-phenylalanine mustard with a four drug combination hexamethylmelamine, cyclophosphamide, methotrexate, and 5-fluorouracil (Hexa-CAF), all patients with minimal residual disease achieved a complete remission with the combination, and six of eight were alive at 5 yr follow-up. Analysis of data indicate that patients with intermediate tumor grades were those who appeared to benefit the most from the Hexa-CAF combination. The use of combination therapy as a second line therapy after alkylating agent failure does not currently appear to be a particularly successful approach. None of the immunotherapy studies has sufficient numbers, duration of follow-up, and analysis of known important prognostic factors to allow a definite conclusion as to the independent contribution of immunotherapy to the treatment of ovarian cancer. (11 Refs)

42. TREATMENT OF OVARIAN CANCER WITH A COMBINATION OF CIS-PLATINUM, ADRIAMYCIN, CYCLOPHOSPHAMIDE AND HEXAMETHYLMELAMINE.

Razis DV, Poulakou E, Petounis A, Papadimitriou G, Kosmides P, Delides G
Diagnostic and Therapeutic Inst. Piraeus, Metaxas Memorial, 51 Botassi St., Piraeus 30, Greece
Oncology; 39(4):205-208 1982

During the last 2 1/2 yr, 38 patients with ovarian cancer were treated with a combination of cis-platinum (CPDD), 50 mg/m2, adriamycin, 30 mg/m2, cyclophosphamide, 300 mg/m2, on Day 1; and hexamethylmelamine (HMM), 6 mg/kg daily, for 14 days. Each course was repeated monthly. Two patients had Stage II, 14 Stage III and 22 Stage IV disease. Fourteen of the 28 patients were previously treated with chemotherapy, 1 with radiation, 6 with both chemotherapy and radiation, and 17 did not have any treatment before CPDD combination. Thirty-one of the 38 cases (81.5%) demonstrated objective responses lasting for 2 mo or more. These responses were partial in 19 and complete in 12 cases. Hematologic toxicity was moderate and with reversible anemia developing in 71% of patients. Gastrointestinal side effects from CPDD were universal. HMM gastrointestinal toxicity necessitated discontinuation of the drug in five patients. Severe nephrotoxicity was observed in two patients but was reversible. There were no drug-related deaths. (Author abstract) (10 Refs)

43. HEXAMETHYLMELAMINE-CAF (CYCLOPHOSPHAMIDE, METHOTREXATE, AND 5-FU) AND CISPLATIN-CAF IN REFRACTORY OVARIAN CANCER.

Sessa C, D'Incalci M, Valente I, Bolis G, Colombo N, Mangioni C
(c/o D'Incalci) Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milano, Italy
Cancer Treat Rep; 66(5):1233-1234 1982

Fifty-three patients (19-73 yr old) with epithelial ovarian cancer not responding to or relapsing while receiving PAC (CP: cisplatin; DX: doxorubicin; and CY: cyclophosphamide) or HAC (HMM: hexamethylmelamine; DX; and CY) regimens received either the combination of HMM (150 mg/square meter po daily on days 1-14) and CAF (CY: 100 mg po daily on days 1-14; MTX: methotrexate: 25 mg/square meter iv on days 1 and 8; and 5-FU: 5-fluorouracil: 300 mg/square meter po daily on days 1-14) or CP (50 mg/square meter iv infusion on day 1) plus CAF. Treatment was repeated every 4 wk. The median number of treatment cycles for the 18 HMM-CAF-treated patients was two. Only 1 of the 18 patients achieved a partial response. Moderate nausea and vomiting were seen in 45% of HMM-CAF patients after 5-FU and MTX administration, stomatitis in 44%, and leukopenia in 50%. Median responses for of CP-CAF-treated patients lasted 7, 7, 10, 11, and 19 mo. The median survival was 14 mo for responders and 6.5

mo for nonresponders. After CP infusion, all 35 patients had severe nausea and vomiting. Thirty-two per cent of the 35 patients had moderate nausea and vomiting after MTX and 5-FU injection on day 8o of treatment. Mucositis was seen in 54% of the CP-CAF patients, leukopenia in 20%, and anemia in 29%. The results indicated that neither CP-CAF nor HMM-CAF should be recommended for the treatment of refractory ovarian cancer. (4 Refs)

44. ADVANCED OVARIAN CANCER: A PROSPECTIVE RANDOMIZED TRIAL OF CHLORAMBUCIL VERSUS COMBINED CYCLOPHOSPHAMIDE AND CIS-DIAMMINEDICHLOROPLATINUM.

Bell DR, Woods RL, Levi JA, Fox RM, Tattersall MH
Oncology Dept., Royal North Shore Hosp. Sydney, St. Leonards, NSW 2065, Australia
Aust NZ J Med; 12(3):245-249 1982

Thirty-seven patients with advanced ovarian cancer were treated in a prospective, randomized trial comparing chlorambucil with a combination of cyclophosphamide and cis-diamminedichloroplatinum (cis DDP). Treatment with the combination was associated with an increased overall response rate (69% versus 23%) ($p = 0.04$). A response was associated with a longer median survival but no survival advantage was demonstrated for patients who received cyclophosphamide/cis DDP. A larger study is needed to evaluate fully the potential of regimens containing cis DDP in the management of advanced ovarian cancer. (Author abstract) (14 Refs)

45. LATE SIDE EFFECTS OF CHEMOTHERAPY IN OVARIAN CARCINOMA. A CYTOGENETIC, HEMATOLOGIC, AND STATISTICAL STUDY.

Einhorn N, Eklund G, Franzen S, Lambert B, Lindsten J, Soderhall S
Dept. Gynecological Oncology, Radiumhemmet Karolinska Hosp., S-104 01 Stockholm, Sweden
Cancer; 49(11):2234-2241 1982

Late side effects of chemotherapy were studied in 51 women who had received at least 300 mg of melphalan for ovarian cancer and had survived for at least 3 yr. Hematologic, statistical, and cytogenetic methods were employed. Six cases of iatrogenic leukemia were found. They appeared to represent a hematologic entity that is fairly difficult to recognize. The risk of iatrogenic leukemia in women who survived for 3 yr or more after melphalan treatment was calculated to be 950 times greater than the leukemia risk in the total female population. The cytogenetic changes were studied with three methods focused on sister chromatid exchange, chromosome aberrations, and DNA damage. The sister chromatid exchange frequency showed a marked increase, but it was corrected within a few mo. Chromosome aberrations expressed by chromosome rearrangements were increased in the peripheral lymphocytes and may persist for several yr. The frequency of DNA strand breaks was decreased indicating the presence of DNA cross-links. Any of these types of genetic alteration could be the initiating event in carcinogenesis. (Author abstract) (31 Refs)

46. THE MULTIMODAL APPROACH TO THE TREATMENT OF STAGE III OVARIAN CARCINOMA.

Fuks Z, Rizel S, Anteby SO, Biran S
Dept. Radiation and Clinical Oncology, Hadassah Univ. Hosp., Kiryat Hadassah, Jarusalem, Israel
Int J Radiat Oncol Biol Phys; 8(5):903-908 1982

A treatment protocol involving sequential application of surgery, combination therapy, second look laparotomy, and whole abdominal irradiation performed to test the feasibility of an aggressive multimodal approach to the treatment of Stage III ovarian carcinoma is discussed. The first of the two-phase study was the induction of remission. After initial surgery, patients were treated with the CHAD combination of chemotherapy (cyclophosphamide, CP; hexamethylmelamine; adriamycin, AD; and cis-dichloroammineplatinum given in monthly repeated courses). If complete resection of residual tumor was not possible, patients continued to receive CHAD chemotherapy until the completion of 14 courses. The second phase of the study was the consolidation of response by whole abdominal irradiation. The whole peritoneal cavity received throughout the course of treatment 3,000 rad in 20 fractions in 4 wk, the pelvis 5,100 rad in 33 fractions in 6-7 wk, and the para-aortic region together with the medial parts of the diaphragms 4,200 rad in 28 fractions in 5-6 wk. Fifteen patients entered the first phase of the study. Four patients did not have a palpable tumor for assessment of response, but did not show any evidence of tumor growth during CHAD therapy. Of the remaining 11 patients, 3 progressed during chemotherapy, whereas others responded with either complete remission (5 patients) or partial response (3 patients) for a total response rate of 8/11 (73%). Ten of 12 patients have had second look laparotomy. The actuarial survival at 2.5 yr from the initiation of chemotherapy was 84%. This is significantly improved compared to a historical control group of Stage III patients treated with a combination of AD and CP chemotherapy. (36 Refs)

47. TREATMENT OF CHILDREN WITH DYSGERMINOMA OF THE OVARY.

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Cancer; 49(12):2608-2611 1982

The therapeutic approach to dysgerminoma, the most common malignant ovarian tumor in children, has been primarily surgical, with radical excision for tumors extending beyond their capsule. Four children with localized disease were treated with limited surgery only and are free of disease. Five others with extensive disease were treated with chemotherapy as the primary therapeutic modality, with or without adjuvant radiotherapy, and three are alive and remain free of disease. Only the two patients with an admixture of other malignant germ cell tumors had recurrence of the other malignant elements after an initial good response. This experience demonstrates pronounced in vivo tumoricidal activity and supports a therapeutic approach to extensive childhood dysgerminoma with an initial chemotherapeutic regimen, resulting in sparing of pelvic and reproductive organs. (Author abstract) (12 Refs)

48. TREATMENT OF ADVANCED OVARIAN CARCINOMA WITH AUTOLOGOUS TUMOR, CORYNEBACTERIA PARVUM AND CHEMOTHERAPY (MEETING ABSTRACT)

Gusdon JP, Homesley HP, Jobson V
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Med Pediatr Oncol; 10(1):99 1982

Fourteen women with advanced (Stage III or IV) ovarian carcinoma of the ovaries have been studied over a 33-month period. Following removal as much of the malignant tissue as possible, the tumor was prepared by separation from normal tissues, irradiated, and stored at 70 C. One week after the surgery, each patient received subcutaneous injections of both

tumor and C Parvum into each inguinal area. Chemotherapy was administered one month later, and immunotherapy and chemotherapy were subsequently done on the 18th and 28th day of each cycle, respectively. After four months of immunotherapy, C Parvum was administered intraperitoneally in the fifth month. Chemotherapy was continued. Patients were tested at intervals with skin tests using C Parvum and autologous tumor. Monitoring of their immune response was done monthly by mitogenic blastogenesis and lymphocyte responses to autologous tumor. Eight patients have died. The longest response has been 33 months, with no evidence of recurrence, and a negative second look. One other patient is alive with no evidence of disease after one year, and four patients are alive with persistent disease after 21-24 months. Measurement of immune parameters has not correlated with their outcome. (no Refs)

49. EPITHELIAL OVARIAN CANCER AND COMBINATION ORAL CONTRACEPTIVES.

Rosenberg L, Shapiro S, Slone D, Kaufman DW, Helmrich SP, Miettinen OS, Stolley PD, Rosenshein NB, Schottenfeld D, Engle RL
Drug Epidemiology Unit, Boston Univ. Sch. Medicine, 777 Concord Ave., Cambridge, MA, 02138
JAMA; 247(23):3210-3212 1982

The risk of epithelial ovarian cancer in relation to the use of combination oral contraceptives was evaluated in a case-control study of women younger than 60 yr. Combination oral contraceptives were used by 35 (26%) of 136 cases and 187 (35%) of 539 controls. The relative risk estimate for combination oral contraceptive use was 0.6 (95% confidence interval, 0.4 to 0.9). The reduction in risk appeared to persist for as long as 10 years after use had ceased and to be greater for longer durations of use, but these results were not statistically significant. The findings were not explained by parity or by other identified potential confounding factors. The results suggest that the use of combination oral contraceptives protects against epithelial ovarian cancer. (Author abstract) (16 Refs)

50. FAMILIAL OVARIAN CARCINOMA.

Borrie PM, Thomson JD
Tauranga Hosp., Tauranga, New Zealand
NZ Med J; 95(703):147-148 1982

Three sisters (65, 47, and 60 yr old) and the 36-yr-old daughter of one of the sisters presented with ovarian carcinoma within a 3-yr period. An aunt of the older women, their mother's sister, had died at age 52 of ovarian cancer. The three older women have one unaffected sister and together have six daughters, including the one already affected. Management of the healthy women may include offering prophylactic oophorectomy with hysterectomy to those whose child-bearing is complete and emphasizing prompt reporting of any suspicious symptoms. (5 Refs)

TROPHOBLASTIC DISEASE

51. CIRCULATING PLACENTAL PROTEINS (HCG, SP1 AND PP5) IN TROPHOBLASTIC DISEASE.

Lee JN, Salem HT, Chard T, Huang SC, Ouyang PC
Dept. Obstretics and Gynecology and Reproductive Physiology, St. Bartholomew's Hosp. Medical Coll, London, England
Br J Obstet Gynaecol; 89(1):69-72 1982

Serum human chorionic gonadotrophin (hCG), pregnancy-specific beta1-glycoprotein (SP1) and placental protein 5 (PP5) levels have been measured by radioimmunoassay in 20 patients (116 samples) with hydatidiform mole, 1 patient (9 samples) with invasive mole and 10 patients (103 samples) with choriocarcinoma. Measurement of both serum SP1 and hCG are useful in the monitoring of these diseases. The presence of PP5 in hydatidiform mole and its absence in choriocarcinoma support the hypothesis that PP5 is closely associated with the invasive activity of malignant trophoblast. (Author abstract) (15 Refs)

52. BRAIN METASTASIS OF CHORIOCARCINOMA.

Kobayashi T, Kida Y, Yoshida J, Shibuya N, Kageyama N
Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, 65 Tsuruma-cho, Showa-ku, Nagoya, Japan
Surg Neurol; 17(6):395-403 1982

Twenty-four patients with histologically verified brain metastasis of choriocarcinoma were analyzed regarding autopsy and operative findings, signs and symptoms, diagnosis, method of treatment, and prognosis. The autopsy incidence of brain metastasis was 66.7% in patients with choriocarcinoma, and the predominance of single brain lesions was confirmed. Most of the metastatic lesions were hemorrhagic. The hemorrhages were intratumoral, peritumoral, and/or subarachnoid. These findings were well correlated with the findings on computed tomographic (CT) scans and the acute onset with rapid progression of symptoms. The history of molar pregnancy, measurements of urinary chorionic gonadotropin, and findings on CT scans were diagnostic. Surgical removal of the lesion followed by chemotherapy combined with irradiation is the treatment of choice in patients with progressive neurological deterioration in whom chemotherapy alone is ineffective. (Author abstract) (19 Refs)

MULTI-SITE STUDIES AND REVIEWS

53. HYPERCALCEMIA ASSOCIATED WITH GYNECOLOGIC MALIGNANCIES. BIOCHEMICAL CHARACTERIZATION.

Stewart AF, Romero R, Schwartz PE, Koborn EI, Broadus AE
Yale Univ. Sch. Medicine, LMP 2074, 333 Cedar St., New Haven, CT
Cancer; 49(11):2389-2394 1982

Fasting calcium excretion, renal phosphorus threshold, plasma 1,25-dihydroxyvitamin D, immunoreactive PTH, nephrogenous cyclic AMP excretion, and tumor burden were assessed in nine patients with gynecologic neoplasms and hypercalcemia. Gynecologic neoplasms were responsible for hypercalcemia in seven of 34 (20.5%) consecutive patients with malignancy-associated hypercalcemia. The tumor burden in each patient was large. Three of four endometrial carcinomas contained squamous elements. All patients displayed biochemical evidence of nonparathyroid humorally mediated hypercalcemia (bone resorption). Treatment of hypercalcemia did not appear to diminish production of the humoral calcemic factor but eradication of tumor eliminated biochemical evidence of the humoral syndrome. It can be concluded that (1) gynecologic neoplasms are a frequent cause of malignancy-associated hypercalcemia, (2) humoral mechanisms appeared to be responsible for the hypercalcemia in 100% of the patients in this series, (3) squamous features occur with unexpected frequency in hypercalcemic endometrial carcinoma, (4) the presence of hypercalcemia connotes a large tumor burden, and (5) treatment direct-

ed at the neoplasm (but not treatment directed at hypercalcemia) may eliminate evidence of ectopic calcemic hormone production. (Author abstract) (30 Refs)

54. INDICATIONS FOR LASER SURGERY IN GYNECOLOGIC ONCOLOGY.

Schellhas HF, Barnes AE
Dept. Obstetrics and Gynecology, Univ. Cincinnati Medical Center, Cincinnati, OH, 45267
Int Adv Surg Oncol; 5:365-384 1982

Carbon dioxide laser (CDL) treatment through the colposcope, tumor vol reduction, and resection of soft tissue malignancies are discussed. Outpatient management is the great advantage of diagnostic colposcopy and endoscopic CDL therapy for female population with abnormal cervical cytology. The procedure is well tolerated without anesthesia or sedation, and bleeding is usually no problem. The zone at risk for the development of cervical intraepithelial neoplasia (CIN) is at the squamo-columnar junction. Only lesions clearly outlined microscopically can be treated. The colposcopically most advanced lesion should be biopsied for diagnostic confirmation. The same patient population diagnosed to have CIN is in part also at risk to have vaginal intraepithelial neoplasia either simultaneously or to develop it later. Since CDL beam can remove a limitless amount of tissue with great precision and since the beam penetrates bone, one of the absolute indications for tissue vaporization is tumor recurring after radiation therapy, which is attached to the bone. Though devised for 'bloodless surgery', CDL beam is absorbed by the layer of blood in a hemorrhaging tumor and becomes inefficient. Hemostasis can be achieved by freezing the tumor tissue using liquid nitrogen spray. The ischemic frozen tissue is then vaporized with the CDL beam. Refreezing is required before the laser beam opens functioning vessels. CDL appears to be the best suited laser for incisional and vaporizing surgical procedures, since the beam is uniformly absorbed by tissue at the wavelength of 10.6 micrometer. (15 Refs)

55. SIMULTANEOUS PRESENTATION OF CARCINOMA INVOLVING THE OVARY AND THE UTERINE CORPUS.

Eifel P, Hendrickson M, Ross J, Ballon S, Martinez A, Kempson R (c/o Hendrickson) Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Cancer; 50(1):163-170 1982

Twenty-nine patients had simultaneous malignant epithelial neoplasms of the uterine corpus and ovary. Three groups were defined on the basis of tumor histology: Group A: those with endometrioid carcinoma in both the uterus and ovary; Group B: those with special variants of corpus carcinoma (papillary, clear cell, mucinous) and identical neoplasms in the ovary; and Group C: those whose uterine and ovarian carcinomas were of dissimilar histologic types. Sixteen women had endometrioid carcinoma in both sites. The median age at diagnosis, 41 yr, was younger than is usual for corpus or ovarian cancer. For all 16 patients, the grade of the ovarian endometrioid carcinoma was similar to that of the endometrioid carcinoma of the uterine corpus. Seven patients had bilateral ovarian neoplasms. Only one patient had myometrial invasion by the corpus carcinoma. No patient with simultaneous ovarian and uterine endometrioid carcinoma, regardless of grade, has died of cancer although one vaginal relapse was treated successfully. This excellent survival of patients with simultaneous endometrioid carcinomas is better than would be expected for either Stage III adenocarcinoma of the endometrium or Stage II ovarian carcinoma. These simultaneously occurring endometrioid neoplasms of ovary and endometrium are considered to be separate primary tumors. The morphologic reasons for this view and therapeutic implications are discussed. In contrast to the patients with endometrioid carcinoma, the eleven patients with other histologic types of carcinoma in the ovary and corpus were older (median age, 61 yr) and more often postmenopausal (90%). These neoplasms were more aggressive, with frequent deep myometrial involvement (63%), tubal involvement (27%), and extension to other pelvic tissues (36%) at the time of initial diagnosis. Six of these 11 patients succumbed to their cancer despite surgical therapy and radiation. The distribution of tumor in some of these patients with nonendometrioid types of carcinoma is suggestive of a single primary with metastases. The (Author abstract) (25 Refs)

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Diagnosis, Treatment

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VULVAR TUMORS

1. STAGE I VULVAR CANCER: CRITERIA FOR MICROINVASION.

Chu J, Tamimi HK, Ek M, Figge DC
(c/o Tamimi) Dept. Obstetrics and Gynecology, Univ. Washington, Univ. Hosp., RH-20, Seattle, WA, 98195
Obstet Gynecol; 59(6):716-719 1982

Thirty-eight women with Stage I epidermoid carcinoma of the vulva were studied retrospectively in an attempt to define the criteria for conservative therapy in early invasive vulvar cancer. Among the 38 women, 23 met the six criteria established for early invasive carcinoma of the vulva. In those 23 women, there were no nodal metastases. Depth of stromal invasion correlated strongly with the degree of tumor differentiation and the presence of carcinoma in situ (CIS). Stromal invasion less than 3 mm and presence of CIS were predictive of no involvement of the lymph nodes or endothelial-like space. (Author abstract) (14 Refs)

2. THE PLACE OF PELVIC EXENTERATION IN THE PRIMARY MANAGEMENT OF ADVANCED CARCINOMA OF THE VULVA.

Cavanagh D, Shepherd JH
Div. Gynecological Oncology, Univ. South Florida Coll. Medicine, Box 18, 12901 N. 30th St., Tampa, FL, 33612
Gynecol Oncol; 13(3):318-322 1982

Over a 25-yr period, 236 patients were treated surgically for carcinoma of the vulva. Of these, 13 (5%) were treated by radical vulvectomy with pelvic exenteration for Stage IV disease. Five of 10 patients (50%) eligible for a 5-yr survival were alive and well with no evidence of disease after this time. None of these five patients had lymph node metastases at the time of her surgery. A review of the English language literature from 1973 to date confirmed that the results with exenteration and radical vulvectomy in selected cases are good. Including our

HE 20.3173/2:

series, a total of 53 patients underwent this procedure, of whom 25 (47%) survived 5 yr. In view of these findings, we feel that consideration should be given to the use of this procedure in patients with advanced, but resectable carcinoma of the vulva. (Author abstract) (9 Refs)

3. MANAGEMENT OF VULVAR INTRAEPITHELIAL NEOPLASIA BY CARBON DIOXIDE LASER.

Townsend DE, Levine RU, Richart RM, Crum CP, Petrilli ES
Cedars-Sinai Medical Tower, 8631 West Third St., Los Angeles, CA, 90048

Obstet Gynecol; 60(1):49-52 1982

Thirty-three patients with vulvar intraepithelial neoplasia were treated with the carbon dioxide (CO_2) laser. In 31 of these patients the lesion was completely eradicated by the laser treatment. All patients experienced moderate pain following the procedure, and two had severe pain. The only other complications were one case of bleeding and one of infection. The CO_2 laser appears to be an acceptable treatment modality for vulvar cancer precursors provided patients are carefully evaluated prior to treatment and invasive carcinoma is ruled out. (Author abstract) (5 Refs)

4. PRIMARY EPIDERMOID CARCINOMA OF THE VULVA.

Lifshitz S, Savage JE, Yates SJ, Buchsbaum HJ
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. Texas Health Science Center, Southwestern Medical Sch., 5223 Harry Hines Blvd., Dallas, TX, 75235

Surg Gynecol Obstet; 155(1):59-61 1982

During a 12 yr period, 102 patients with invasive epidermoid carcinoma of the vulva were treated at the University of Iowa Hospitals and Clinics. The over-all corrected 3 yr survival rate was 65.5%, or 67 of 102 patients. Those treated by radical vulvectomy and bilateral dissection of groin nodes had a 3 yr survival rate of 76.9%, or 40 of 52 patients,while those treated by radiotherapy had a survival rate of 10%, or 2 of 20 patients. Those with Stage I disease lesions, less than 1 cm in diameter, had an excellent survival rate whether they were treated by vulvectomy only or by radical vulvectomy with groin node dissection. Our experience in this selected group of patients would indicate that a degree of individualization in the treatment of early invasive lesions of the vulva can give most satisfactory results. (Author abstract) (4 Refs)

5. MALIGNANT MELANOMA OF THE VULVA: REPORT OF 18 CASES.

Bouma J, Weening JJ, Elders A
Dept. Obstetrics and Gynecology, Univ.Hosp. Groningen, Oostersingel 59, 9713 EZ Groningen, The Netherlands

Eur J Obstet Gynecol Reprod Biol; 13(4):237-251 1982

Clinical and pathological data of 18 patients (40-90 yr old, av 64 yr) with melanoma of the vulva are reviewed. Nodular melanoma was found in 13/16 with primary tumor while 3 had a superficial spreading melanoma associated with dermal invasion. The therapy of choice was radical vulvectomy (11 patients) with en bloc dissection of inguinal and femoral nodes. Among 9/16 patients evaluable for 5-yr survival, 5 had no evidence of disease, 3 died with tumor growth, and 1 died probably of cardiac disease. (26 Refs)

VAGINAL TUMORS

6. SQUAMOUS CELL CARCINOMA OF THE VAGINA: A CLINICAL STUDY OF THE LOCATION OF THE TUMOR.

Houghton CR, Iversen T
(c/o Iversen), Norwegian Radium Hosp., Montebello, Oslo 3, Norway

Gynecol Oncol; 13(3):365-372 1982

Sixty-seven cases of primary squamous cell carcinoma of the vagina were treated between 1956 and 1975. Irradiation was the principal mode of therapy and overall 5-yr survival was 38.8%. Lesions involving the lower vagina had a propensity for metastasis, particularly to the inguinofemoral nodes. Radical surgery is suggested for selected cases with lesions of the upper third or the posterior wall of the vagina with removal of the inguinofemoral nodes where appropriate. (Author abstract) (13 Refs)

7. TREATMENT OF VAGINAL CARCINOMA IN SITU WITH THE CARBON DIOXIDE LASER.

Townsend DE, Levine RU, Crum CP, Richart RM
Cedar Sinai Medical Tower, 8631 West Third St., Los Angeles, CA, 90048

Am J Obstet Gynecol; 143(5):565-568 1982

Thirty-six patients with vaginal intraepithelial neoplasia were treated with the carbon dioxide laser. More than half of the patients had Grade 3 vaginal intraepithelial neoplasia (carcinoma in situ). The majority of patients were treated in a single session; six patients were treated twice, and two patients were treated three times. In 92% of the patients, the lesions were completely removed by the laser without significant side effects. (Author abstract) (8 Refs)

8. DEVELOPMENT OF CLEAR CELL ADENOCARCINOMA IN DES-EXPOSED OFFSPRING UNDER OBSERVATION.

Kaufman RH, Korhonen MO, Strama T, Adam E, Kaplan A
Dept. Obstetrics and Gynecology, Texas Medical Center, Houston, TX, 77030

Obstet Gynecol; 59(6,Suppl):68S-72S 1982

Two cases of clear cell adenocarcinoma of the vagina detected at follow-up in young women exposed in utero to diethylstilbestrol are reported. One patient, aged 23, had been followed for 2 yr before carcinoma was diagnosed; the second patient, aged 22, had been seen on a regular basis for 5 yr, 8 mo. In both instances, suspicion of the presence of carcinoma was aroused by the palpation of a small nodule in the vaginal fornix. Hysterosalpingography was performed on both patients and, in one instance, an abnormal x-ray film was reflected by the gross appearance of the uterine cavity found in the surgical specimen. (Author abstract) (7 Refs)

CERVICAL AND UTERINE TUMORS

9. CONTACT HYSTEROSCOPIC EVALUATION OF THE ENDOCERVIX AS AN ADJUNCT TO COLPOSCOPY.

Baggish MS, Dorsey JH
Dept. Obstetrics and Gynecology, Mount Sinai Hosp., 500 Blue Hills Ave., Hartford, CT, 06112
Obstet Gynecol; 60(1):107-110 1982

A total of 66 women with cervical intraepithelial neoplasia extending into the endocervical canal were investigated by endocervical curettage, contact endoscopy, and conization biopsy of the cervix. Although atypical epithelium was obtained in only 8 women by blind endocervical curettage, contact endoscopy identified 42 instances of disease of equal or greater magnitude than determined by the original ectocervical colposcopic evaluation. These findings were subsequently confirmed by conization biopsy. As the 6-mm contact hysteroscope may easily be inserted into the pregnant cervix, sufficient reassurance may be gained to avoid endocervical curettage or cone biopsy and thus to avoid the hazard of major hemorrhage and/or pregnancy interruption. (Author abstract) (11 Refs)

10. EFFECT OF CYTOLOGIC SCREENING ON THE DETECTION OF CERVICAL CARCINOMA.

Yajima A, Mori T, Sato S, Wakisaka T, Suzuki M
Dept. Obstetrics and Gynecology, Tohoku Univ. Sch. Medicine, 1-1 Seiryo-Machi, Sendai 980, Japan
Obstet Gynecol; 59(5):565-568 1982

An investigation has been made of the relationship between the histologic features of detected cancers of the uterine cervix and the history of previous cervical screening in 732 cases. Six hundred forty-nine of 732 (88.7%) cases with cancers of the uterine cervix were from the group of unscreened women, whereas only 83 cases (11.3%) were from the group of screened women. Frank invasive carcinoma was found in 21.0% (136 cases) of the former group and in only 3.6% (3 cases) of the latter. Adenocarcinoma of the uterine cervix was found in 0.3% (21 cases) of the unscreened women and in 7.2% (6 cases) of the screened women. Among the women who had undergone cervical screening within 3 yr prior to a histologically confirmed diagnosis, invasive carcinoma (excluding adenocarcinoma) was found in 23.3% (14 of 60 women), whereas carcinoma in situ was found in 76.7%. This ratio (1:4) of invasive carcinoma to carcinoma in situ was found to be unchanged among the women of this group regardless of whether the interval from the previous screening was 1, 2, or 3 yr. In contrast, when the interval between screenings was 4 or more yr, the ratio of invasive carcinoma increased to 52.9% (9 of 17 cases). (Author abstract) (14 Refs)

11. PAIRED CERVICAL SMEARS: A METHOD OF REDUCING THE FALSE-NEGATIVE RATE IN POPULATION SCREENING.

Bellby JO, Bourne R, Guillebaud J, Steele ST
Bland Sutton Inst. Pathology, Middlesex Hosp. Medical Sch., London W1P 7PP, England
Obstet Gynecol; 60(1):46-48 1982

Cervical smears taken by the wooden Ayre spatula (widely used in the United Kingdom) and by a plastic spatula (Armovical) were compared for their ability to detect dysplastic cervical epithelium and endocervical cells. At the same time, the value of taking duplicate smears was assessed. Paired cervical smears were obtained at a single attendance from 21,352 women, using the two types of spatulas in four different sequences. Although individually the Armovical proved superior to the Ayre spatula for the collection of endocervical epithelial material, this advantage was not complemented by any marked improvement in its detection of cervical dysplasia. Paired smear sampling, however, was clearly more rewarding in this respect and also allowed the introduction of laboratory quality control, as each preparation of any given pair was examined by a different screener. The false-negative rate was 18.5%: it comprised 11.1% sampling error and 7.4% screening error. It is concluded that paired smear sampling in population screening would significantly reduce the false-negative rate. (Author abstract) (15 Refs)

12. ARE THE HISTOLOGICAL AND ULTRASTRUCTURAL FEATURES OF ENDOMETRIAL CARCINOMAS RELIABLE INDICATORS OF THEIR STEROID RECEPTOR CONTENT?

Genton CY, Buchi KA
Institut fur Pathologie der Universitat Zurich, Universitatsspital, CH-8091 Zurich, Switzerland
Gynecol Obstet Invest; 13(4):213-225 1982

Histological and ultrastructural features of endometrial carcinomas were studied in 15 postmenopausal patients to correlate the steroid receptor content with endometrial carcinoma. All but one tumor in the study contained one or both steroid receptors. Two neoplasms displayed no measurable estrogen-binding capacity but presented progesterone receptors in small amounts. In a poorly differentiated carcinoma, the high level of circulating estrogens may explain the fact that the search for estrogen receptors remained negative. In a tumor of moderate differentiation, the serum estradiol was very low suggesting that the neoplasm effectively displayed no estrogen-binding capacity. (20 Refs)

13. THE PROGNOSTIC VALUE OF CEA DETERMINATIONS IN THE PLASMA OF PATIENTS WITH SQUAMOUS CELL CANCER OF THE CERVIX.

Kjorstad KE, Orjasaester H
Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Cancer; 50(2):283-287 1982

One hundred and ninety-five patients with squamous cell cancer of the cervix have been followed for 2-4 yr. Pretreatment CEA determination was of prognostic value only in patients with early clinical disease. Serial determinations of CEA after primary treatment are of limited value in advanced stages. Sixty-five percent of patients developing recurrent cancer after initial therapy for Stage IB disease had plasma CEA levels exceeding 5.0 ug/l. In many of these cases the CEA elevation preceded the clinical diagnosis by several months. (Author abstract) (15 Refs)

14. CIRCULATING IMMUNOCOMPLEXES IN THE SERUM OF PATIENTS WITH CANCER OF THE UTERINE CERVIX.

Vodvarka P, Willaschek J, Lochman I, Vrtna L
Radioterapeut. odd., KNsP, Nadrazni 1, 739 21 Ostrave-Paskov, Czechoslovakia
Cesk Gynekol; 47(4):272-278 1982

The serum levels of circulating immunocomplexes (CI) were determined in 25 women (27-81 yr old, av age 51.8 yr) with carcinoma of the uterine cervix by precipitation with polyethylene glycol. Spinocellular carcinoma was diagnosed in 23/25 patients, anaplastic carcinoma in 1/25. Twenty of the 25 pa-

tients were subjected to diagnostic surgery before radiotherapy, four others to hysterectomy with bilateral adnexectomy. The av IC level for all 25 patients was found to be 63.4 +-26.5 units (U), which is significantly higher than in the normal population. The CI levels found before radiotherapy were 50.7 U in the 7/25 patients in Stage T2, 65.9 in patients in Stage T3 and 110 U in 1 patient with Stage T4. The CI levels, determined in 21 women followed up for 1.1-19.4 yr after radiotherapy, were 55.8 U in 7/21 patients followed up for up to 2 yr and 45.7 U in 14/21 patients followed up for more than 2 yr. The CI levels in these 21 patients were 38.3 U in 8 patients in Stage T1, 59.3 U in 7 patients in T2 and 37 U in 6 patients in T3. The CI levels were consequently reduced in irradiated patients and patients surviving more than 2 yr, but still significantly higher than the normal values. (24 Refs) (In CZE)

15. PRIMARY SURGICAL TREATMENT IN ONE HUNDRED NINETY-FIVE CASES OF STAGE IB CARCINOMA OF THE CERVIX.

Allen HH, Nisker JA, Anderson RJ
111 Waterloo St., London, Ontario N6B 2M4, Canada
Am J Obstet Gynecol; 143(5):581-584 1982

Stage IB carcinoma of the cervix may be treated primarily by either radiotherapy or operation. A primary surgical approach was used in 95 patients for the following indications: young age with desire to retain ovarian function (124), pelvic inflammatory disease (33), pregnant or post partum (15), refusal of radiotherapy (11), anatomic problems contraindicating radiotherapy (10), undiagnosed pelvic mass (7), verrucous tumor (3), mucus-secreting tumor (2), syphilis (1), and previous radiotherapy for Hodgkin's disease (1). Twelve patients had two indications. The surgical procedures were radical abdominal hysterectomy and pelvic lymph node dissection (191) and Schauta-Amreich (radical vaginal) hysterectomy (4). Fourteen patients had serious postoperative complications. The uncorrected 5-yr survival rate (95.1% follow-up) was 91.1%. The rationale for recommending a primary surgical approach to selected patients with Stage IB cervical carcinoma is presented. (Author abstract) (17 Refs)

16. TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA WITH THE CARBON DIOXIDE LASER: REPORT OF 543 PATIENTS.

Anderson MC
Dept. Histopathology and Colposcopy, Samaritan Hosp. Women, Marylebone Road, London NW1 5YE, England
Obstet Gynecol; 59(6):720-725 1982

Five hundred forty-three patients with cervical intraepithelial neoplasia were treated with the carbon dioxide laser and 441 have been seen for follow-up. The success rate was 76.4% after one treatment and 98% after two treatments. Many patients who returned with apparent minor abnormalities at the first follow-up visit had normal colposcopic results and Papanicolaou smears 6 mo later. The complication rate was low, and no significant problems were caused by pain or bleeding at the time of treatment. Postoperative hemorrhage requiring hospital admission occurred in 1% of patients. Laser treatment should be carried out only in departments with colposcopic expertise. (Author abstract) (13 Refs)

17. WHOLE PELVIC IRRADIATION IN STAGE I ENDOMETRIAL CARCINOMA: CHANGES IN NUMBERS AND REACTIVITIES OF SOME BLOOD LYMPHOCYTE SUBPOPULATIONS.

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Tissue Typing Lab., Rikshospitalet, Natl. Hosp., Oslo, Norway
Gynecol Oncol; 13(3):283-292 1982

Peripheral blood lymphocytes of 64 operated, Stage I endometrial carcinoma patients were tested for natural killer (NK) activity, mitogenic (PHA) responsiveness, and distribution of surface markers. Sequential studies showed an 83% reduction of lymphocyte numbers immediately after 4,000 rad whole pelvic irradiation. T cells were relatively more sensitive to in vivo irradiation than NK cells. The long-term effects were studied in patients belonging to a clinical trial and who were either randomized to radiotherapy or not. Three to 5 yr after treatment, the irradiated patients showed increased NK activity and a greater fraction of lymphocytes bearing receptors for the Fc part of immunoglobulin G, as compared to controls. Conversely, lymphocytes from radiotherapy patients showed a depressed PHA responsiveness, which could be attributed to T-cell depletion. When investigated 9-12 yr after treatment, the results of functional tests and cell enumerations were similar for the two treatment groups. It is concluded that this radiotherapy regime causes long-lasting, although transitory, depletions of certain blood lymphocyte subpopulations. On a per cell basis, however, the lymphocytes have retained their functional capacity. (Author abstract) (21 Refs)

18. A PHASE I STUDY OF MISONIDAZOLE AND PELVIC IRRADIATION IN PATIENTS WITH CARCINOMA OF CERVIX.

Thomas GM, Rauth AM, Black BE, Cummings BJ, Sorenti VL, Bush RS
Dept. Radiation Oncology, Ontario Cancer Inst., Princess Margaret Hosp., Toronto, Ontario M4X 1K9, Canada
Br J Cancer; 45(6):860-868 1982

A Phase I study of oral daily misonidazole (MISO) with conventional pelvic irradiation, has been conducted in patients with carcinoma of the cervix Stages IB, IIB, IIIB and IVA. MISO was administered in daily dosages to sequential groups of patients at doses of 0.15 g/m2, 0.30 g/m2 or 0.45 g/m2 for 22 days over 5 wk. Sixteen patients were assigned to each dose level. Using a double-blind randomization, they received either placebo (3/16) or MISO (13/16). The major dose-limiting toxicity was peripheral neuropathy (PN). None of the 13 patients receiving 0.15 g/m2 or the 13 receiving 0.3 g/m2 developed PN. However, 6/13 at the 0.45 g/m2 level (total dose less than or equal to 9.9 g/m2) developed PN. Additional patients were entered at this level and a total of 13/26 developed PN, which was considered of clinically significant severity in 9. Symptoms of PN have persisted from 1 wk to 10 mo, and have been completely reversed in 9/13 patients. Pharmacological parameters were examined for correlation with clinically evident toxicities. Although peak plasma MISO levels and half-lives did not correlate significantly with PN, there was a significant correlation between the calculated 'area under the curve' (AUC) and PN. No correlation exists between PN and total urinary excretion of MISO or the O-demethylation product. A daily dose of 0.45 g/m2; MISO (total dose less than or equal to 9.9 g/m2) is considered to produce an acceptable level of toxicity for this patient population. (Author abstract) (18 Refs)

19. PREOPERATIVE RADIUM INSERTION IN THE MANAGEMENT OF CARCINOMA OF THE ENDOMETRIUM.

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Geburtshilfe Frauenheilkd; 42(5):394-396 1982

From 1966-1975 202 women with carcinoma of the endometrium Stage I and Stage II received intracavitary preoperative radiotherapy in a dosage of 300 mgeh. The statistical analysis compared to patients who received primary operation without radiotherapy showed no difference in the 5 yr survival rate nor in the incidence of vaginal, pelvic side wall, and distant metastases. Preoperative radiotherapy is only an additional stress on the patients. (Auth r abstract) (34 Refs) (In GER)

20. STEREO X RAY PHOTOGRAMMETRY APPLIED FOR PREVENTION OF SIGMOID-COLON DAMAGE CAUSED BY RADIATION FROM INTRAUTERINE SOURCES.

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Int J Radiat Oncol Biol Phys; 8(6):1011-1017 1982

Details of the application technique and stereo x-ray photogrammetry (SRM) used to prevent severe sigmoid-colon radiation lesions in the radiation therapy of carcinoma of the uterine cervix are presented. Most late complications at the sigmoid-colon and also at the gut appear 1-2 yr following treatment. Follow-up data of all cervix carcinoma patients treated with intrauterine applications between 1973-1976 were reviewed. None of the patients required surgical intervention for radiation damage. The rate of local failures was studied in patients with Stage I, II, or III carcinoma of the cervix. The local failure did not significantly increase when, according to SRM dosimetry, the treatment was modified to prevent radiation damage. When readings from LiF probes inserted into the recto-sigmoid bowel were compared with direct readings (gamma-meter) and with results of SRM measurements at the barium filled sigmoid-colon, large discrepancies were observed. Observed differences could have been caused by the fact that the thermoluminescence method has been applied as an integrating measurement lasting 3 hr and the position of the probe may be changed during that time; whereas the SRM measurement only refers to the moment at which the films have been exposed. Experience with greater than 200 insertions with LiF elements indicated that rectal probes are not suitable for routine sigmoid-colon dosimetry. (9 Refs)

21. CARCINOMA OF THE ENDOMETRIUM III. ANALYSIS OF 865 CASES OF ADENOCARCINOMA AND ADENOACANTHOMA.

Connelly PJ, Alberhasky RC, Christopherson WM
(c/o Christopherson) Dept. Pathology, Sch. Medicine, Health Sciences Center, Univ. Louisville, Louisville, KY, 40292
Obstet Gynecol; 59(5):569-575 1982

Eight hundred sixty-five patients with confirmed adenocarcinoma of the endometrium were studied. Eight hundred eleven were followed up for at least 5 yr or until death, and 537 were followed up for 10 yr. The survival rate was 77.1% at 5 yr and 61.0% at 10 yr. Age at diagnosis was the single most important clinical determinant of survival. Tumor grade was an important predictor of the course of disease, and nuclear grade was a significantly more accurate indicator than was histologic grade. Stage and depth of invasion were also important predictors of survival. The 5-yr survival rate for black women was only 41.9%. Stage for stage and grade for grade, women undergoing hysterectomy alone and with radiation had similar survival rates. Adenoacanthoma had a better prognosis than did adenocarcinoma without squamous metaplasia; there were no deaths at 5 or 10 yr in women diagnosed before age 50. The subtype of carcinoma was found to be a highly significant predictor of prognosis. (Author abstract) (32 Refs)

22. ADENOCARCINOMA OF THE ENDOMETRIUM: ANALYSIS OF 256 CASES WITH CARCINOMA LIMITED TO THE UTERINE CORPUS. PATHOLOGY REVIEW AND ANALYSIS OF PROGNOSTIC VARIABLES.

Hendrickson M, Ross J, Eifel PJ, Cox RS, Martinez A, Kempson R
Dept. Pathology and Radiology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Gynecol Oncol; 13(3):373-392 1982

Histologic specimens of all patients undergoing hysterectomy for clinical Stage I adenocarcinoma of the endometrium at Stanford University Hospital between 1959 and 1975 were reexamined. From this group 256 acceptable cases of adenocarcinoma confined to the uterine corpus (Pathologic Stage I) were identified. In patients treated with initial surgery, relapse rate was highly correlated with depth of myometrial invasion ($p = 0.0001$) and also with the histologic grade of the uterine adenocarcinoma ($p = 0.008$). Twenty six patients (10%) had lesions with papillary architecture and anaplastic cytology similar to papillary serous carcinoma of the ovary. These women with uterine papillary serous carcinoma (UPSC) had a 50% relapse rate and accounted for one-half the treatment failures (13/26) in the entire study group. Six of the seven upper abdominal relapses in this study were in patients with UPSC, suggesting that this histologic variant may behave more like ovarian serous carcinoma than the usual endometrial adenocarcinoma. Twenty one patients (9%) had endometrial carcinomas with extensive mucinous differentiation (mucinous carcinoma), while 38% of all the cases of endometrial carcinoma showed at least some focal mucin production. Twenty percent showed focal squamous differentiation. Neither mucinous nor squamous differentiation, as we have applied these designations, were significantly correlated with relapse rate. Among the patients undergoing hysterectomy for clinical Stage I adenocarcinoma, 99 patients were found on review to have lesions which fell short of our current criteria for diagnosis of carcinoma in the uterine corpus and were reinterpreted as metaplasia and/or hyperplasia. None of these patients subsequently developed clinical relapse. The results of this study suggest a need for modification in the FIGO grading system for endometrial cancer and also support a definition of well-differentiated endometrial carcinoma more restrictive than that commonly employed. (Author abstract) (41 Refs)

23. MANAGEMENT OF STAGE I CARCINOMA OF THE UTERUS.

Paterson E, Spratt D, Tomkiewicz Z, Lewis C, Rathbun P
Dept. Radiation Oncology and Nuclear Medicine, Rochester General Hosp., 1425 Portland Ave., Rochester, NY, 14621
Obstet Gynecol; 59(6):755-758 1982

In an attempt to limit the use of adjuvant irradiation in the management of Stage I endometrial carcinoma to high-risk patients only, a protocol was developed that utilizes grading and degree of myometrial invasion as indicators of high risk. From 1974 to 1977, 140 patients at Rochester General Hospital were treated according to this protocol. All patients had total ab-

dominal hysterectomy and bilateral salpingo-oophorectomy. Adjuvant irradiation was given only to the patients who had Grade 3 curettings or greater than one third myometrial invasion. In this series only 20.7% required irradiation. There were no vaginal or pelvic recurrences and the 5-yr tumor-free survival rate was 93%. (Author abstract) (17 Refs)

24. ADENOCARCINOMA OF THE UTERINE CERVIX.

Tamimi HK, Figge DC
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. Washington Sch. Medicine, Seattle, WA, 98195
Gynecol Oncol; 13(3):335-344 1982

Adenocarcinoma of the cervix represented 12.7% of all cervical carcinoma seen at the University of Washington. The mean age of 66 patients with adenocarcinoma of the cervix was not significantly different from the mean age of those with squamous cell carcinoma and was 43.6 (range 15-83). 76% of the patients were assigned to Stage I disease. Stage II disease was diagnosed in 15% and Stages III-IV represented 9%. The pathologic diagnosis included adenocarcinoma in 50 patients, adenosquamous carcinoma in 9, clear cell carcinoma in 5, and adenoid cystic carcinoma in 2. The survival rate was directly related to the stage of disease and to the presence or absence of lymph node metastasis. The recurrence rate was significantly higher in adenocarcinoma of the cervix with node metastasis when compared with a similar group of patients with squamous cell carcinoma. (Author abstract) (10 Refs)

25. VAGINAL RECURRENCE OF ADENOCARCINOMA OF THE ENDOMETRIUM.

Phillips GL, Prem KA, Adcock LL, Twiggs LB
Dept. Obstetrics and Gynecology, Div. Gynecologic Oncology, Univ. Minnesota Medical Sch., Minneapolis, MN, 55455
Gynecol Oncol; 13(3):323-328 1982

During a 28-yr period, 949 patients were treated for adenocarcinoma of the endometrium at the University of Minnesota Hospitals. Eighty-one of these patients presented with vaginal recurrence. The incidence of vaginal recurrence for patients receiving primary therapy at this institution was 0.9%. Sixty-nine percent of patients presented with vaginal bleeding, but 22% were asymptomatic. Seventy-three percent of patients eventually died of disease. Seventy-five percent of recurrences occurred within 3 yr of primary therapy, but much longer intervals were noted. In patients with isolated vaginal recurrences, the interval to recurrence directly correlated with survival (p less than 0.0005). The poor outcome of these patients indicates a need for evaluation of adjuvant therapy. (Author abstract) (13 Refs)

26. EVIDENCE FOR AN ASSOCIATION BETWEEN CHLAMYDIA TRACHOMATIS AND CERVICAL INTRAEPITHELIAL NEOPLASIA.

Hare MJ, Taylor-Robinson D, Cooper P
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Br J Obstet Gynaecol; 89(6):489-492 1982

The endocervices of 206 women with cervical intraepithelial neoplasia (CIN) and 13 with cancer of the cervix were examined for Chlamydia trachomatis, Mycoplasma hominis and Ureaplasma urealyticum. A group of 103 women with other gynecological problems acted as controls. C trachomatis was found in a significantly greater proportion of women with CIN (8.2%; 16/196) or cervical cancer (18.2%; 2/11) than in controls (1%; 1/97). In contrast, incidence of M hominis was 24.7%, 53.8% and 21.3%, and that of U urealyticum 72.3%, 46.2% and 60.2%, respectively, in the same groups. Lymphoid follicles, previously reported to be associated with chlamydial infection, were found in 9/26 cone biopsy or hysterectomy specimens which showed evidence of CIN, whereas no such follicles were found in 39 cervices without evidence of CIN. The possible relationship between infection with C trachomatis and sexual activity is discussed. (26 Refs)

27. GENITAL WARTS AND CERVICAL CANCER. I. EVIDENCE OF AN ASSOCIATION BETWEEN SUBCLINICAL PAPILLOMAVIRUS INFECTION AND CERVICAL MALIGNANCY.

Reid R, Stanhope CR, Herschman BR, Booth E, Phibbs GD, Smith JP
Dept. Obstetrics and Gynecology, Sinai Hosp. Detroit, 6767 West Outer Drive, Detroit, MI, 48235
Cancer; 50(2):377-387 1982

A blind comparative survey was undertaken to study the prevalence of subclinical papillomavirus infection (SPI) in a representative sample of women treated surgically for invasive or preinvasive cervical neoplasia. According to a semiobjective rating system, 73 of 80 women (91%) with cervical neoplasia and 10 of 80 matched controls (12.5%) showed histological evidence of human papillomavirus (HPV) infection. Sixty of the controls (75%), but none of the study group, had normal cervicovaginal epithelium. A highly significant statistical relationship exists between subclinical papillomavirus infection of the lower genital tract and the occurrence of cervical neoplasia ($F = 378$; p less than 0.001; $x2 = 109$, p less than 0.001). The prevalence of SPI was 7x greater in the study group than in comparable controls of equivalent disease status. Because both are covariables of promiscuity, statistical associations exist between cervical neoplasia and all sexually transmitted diseases. However, the strength, specificity and consistency of this relationship suggest that SPI may be a precursor of cervical malignancy. This contention is given biologic plausibility by a broad fabric of supporting epidemiologic, virologic and clinocopathologic evidence. (Author abstract) (58 Refs)

28. SURVIVAL AMONG WOMEN WITH ENDOMETRIAL CANCER: A COMPARISON OF ESTROGEN USERS AND NONUSERS.

Chu J, Schweid AI, Weiss NS
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Am J Obstet Gynecol; 143(5):569-573 1982

In order to determine the role of postmenopausal estrogen use in survival of patients with endometrial cancer, we identified, through a population-based tumor registry serving the area, all white women in King County, Washington, aged 50 to 74, who developed endometrial cancer between January, 1975, and April, 1976 ($N = 363$). Estrogen use prior to diagnosis and survival status were ascertained through personal interview, medical records of private physicians, and registry follow-up data. The 4-yr relative survival ratio in estrogen users was 1.05 compared to 0.898 in nonusers. Overall, after adjustment for age, the survival in estrogen users was significantly better than in nonusers ($Chi2 = 30.5$; p much less than 0.0001). While estrogen use may predispose to an increased incidence of endometrial cancer, it appears that such use does not lead to increased mortality from this condition. (Author abstract) (25 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

29. COMPUTED TOMOGRAPHY IN OVARIAN CARCINOMA: PATTERNS OF DISEASE AND LIMITATIONS.

Mamtora H, Isherwood I
Dept. Diagnostic Radiology, Univ. Manchester, Stopford Building, Oxford Road, Manchester, England
Clin Radiol; 33(2):165-171 1982

Between June 1977 and July 1980, a mixed group of 46 patients with ovarian carcinoma was examined by computed tomography (CT). CT was useful for the demonstration of extent of disease within the abdomen and pelvis and may be used to provide an objective means for assessing response to treatment. The limitations of CT include failure to detect peritoneal deposits less than 2-3 cm in diameter, bowel infiltration and minor residual or recurrent disease. The patterns of disease as seen on CT are illustrated and its potential role is discussed. (Author abstract) (15 Refs)

30. LIMITATIONS OF THE CLONAL AGAR ASSAY FOR THE ASSESSMENT OF PRIMARY HUMAN OVARIAN TUMOUR BIOPSIES.

Bertoncello I, Bradley TR, Campbell JJ, Day AJ, McDonald IA, McLeish GR, Quinn MA, Rome R, Hodgson GS
Biological Res. Unit, Cancer Inst., 481 Little Lonsdale St., Melbourne, Victoria, 3000, Australia
Br J Cancer; 45(6):803-811 1982

One hundred and fourteen biopsy specimens from 70 patients with ovarian carcinoma at all stages of diseases were submitted for assessment of clonogenic capacity in agar. A highly significant correlation was found between agar clonogenicity and patient survival after biopsy. However, problems related to inherent tumor heterogeneity, quality of sample and tissue disaggregation indicate that this technique may have limited applicability in the routine assessment of patients. Only 41 biopsy specimens (36%) from 31 patients (44.3%) complied with the prerequisite criteria for agar clonogenic assessment, namely: (a) the confirmed presence of malignant cells in the biopsy, (b) the ability to prepare a single-cell suspension, and (c) adequate viable cell numbers for assay. Furthermore, although the dominant patterns of agar clonogenic growth could be identified and correlated with stage of disease, the heterogeneity in both initial clonogenic capacity and 'self-renewal' capacity assessed by the ability of primary clones to propagate in liquid culture and reclone in agar was too inconsistent for the assay to be used as a prognostic index for the individual patient. (Author abstract) (29 Refs)

31. DENSITY/VOLUME ANALYSIS IN THE STUDY OF CELLULAR HETEROGENEITY IN HUMAN OVARIAN CARCINOMA.

Mackillop WJ, Stewart SS, Buick RN
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Br J Cancer; 45(6):812-820 1982

A method is presented for the description of a heterogeneous cell population with respect to the vol and density of its cellular components, based on computer analysis of the cell-vol spectra of density-gradient fractions. Display programs were developed to produce either a perspective plot or an isofrequency contour plot ('fingerprint') of the two-parameter data. The use of sequential density and velocity gradients permitted the separation and study of the properties of any subpopulation. We describe the results of an analysis of cellular heterogeneity in an ovarian carcinoma cell line and in two cases of ascites cells from human ovarian carcinoma. The proliferative state (labeling index) and growth potential (culture clonogenicity) of cells from one malignant ascites have been 'mapped' in terms of density/vol parameters. The results are discussed in terms of their impact on the view of human ovarian carcinoma as a stem-cell system. (Author abstract) (9 Refs)

32. MALIGNANT NEUROECTODERMAL TUMOR OF THE OVARY, A DISTINCTIVE FORM OF MONODERMAL TERATOMA. REPORT OF FIVE CASES.

Aguirre P, Scully RE
(c/o Scully) Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Am J Surg Pathol; 6(4):283-292 1982

Five cases of malignant neuroectodermal tumor of the ovary are described. Four of the tumors were primary, two of them pure and two almost pure; the fifth case was originally thought to be primary but autopsy findings suggested that it was adrenal in origin. Presenting symptoms in the four patients (13-17 yr old) with primary tumors included an abdominal mass, abdominal enlargement, and abdominal pain. All four tumors were unilateral; two were Stage Ia, one Stage IIa, and one Stage III. The primary tumors ranged from 15 to 20 cm in diameter. Two specimens were predominantly solid, containing only small cysts, while two others were predominantly cystic. At microscopic examination all four tumors contained masses of undifferentiated small cells showing slight to marked nuclear pleomorphism with tumor giant cell formation. The four tumors showed focal differentiation in the direction of glial tissues. In 4/5 of the patients, the tumors were misdiagnosed as acute appendicitis or ovarian cysts following preliminary examinations. Difficulties in diagnosing primary malignant neuroectodermal tumors of the ovary are discussed. (17 Refs)

33. OVARIAN MUCINOUS TUMORS WITH FOCI OF ANAPLASTIC CARCINOMA.

Prat J, Young RH, Scully RE
(c/o Young) Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02116
Cancer; 50(2):300-304 1982

Four ovarian mucinous cystic tumors that contained solid nodules of anaplastic carcinoma in their walls are described. All the tumors had metastasized at the time of or shortly after operation and two have already proven fatal. The anaplastic nodules may be confused on gross and microscopic examination with sarcomas and sarcoma-like nodules, both of which may also be encountered in the wall of mucinous cystic tumors. Although the distinction of foci of anaplastic carcinoma from foci of sarcoma may not have prognostic significance, both of them should be separated from sarcoma-like nodules because of the favorable prognosis associated with the latter. In favor of a diagnosis of anaplastic carcinoma are poor circumscription of the nodules, vascular invasion and absence of a prominent inflammatory reaction with multinucleated giant cells of the epulis type. (Author abstract) (3 Refs)

34. IMMUNOCHEMICAL DEMONSTRATION OF AN OVARIAN CANCER-ASSOCIATED URINARY PEPTIDE.

Stenman UH, Huhtala ML, Koistinen R, Seppala M
I, II Dept. Obstetrics and Gynecology, Helsinki Univ. Central Hosp., SF-00290 Helsinki 29, Finland
Int J Cancer; 30(1):53-57 1982

Immunization with a peptide fraction from ovarian cancer urine resulted in an antiserum that reacts with a 6,000-dalton (6K) peptide. In urine from some patients with advanced gynecological cancer, the concentration of 6K peptide was high enough to be detected by immunodiffusion. By radioimmunoassay the levels in normal serum could be determined. The concentration in serum was 5-20 ug/l and that in urine 5-50 ug/l. Elevated levels were observed in urine from 5 out of 8 patients with ovarian cancer, 10 out of 14 patients with cervical cancer and 9 out of 14 patients with endometrial cancer. The highest level observed was 12,000 ug/l. High concentrations of the 6K peptide (100-300 ug/l) were observed in amniotic fluid from 14-16 weeks of pregnancy. Some tumor extracts also had a high concentration of the 6K peptide. No immunological relationship was observed between the peptide and known tumor-associated antigens or serum proteins. These results suggest that the peptide is a new oncodevelopmental peptide which may have significance as a tumor marker. (Author abstract) (17 Refs)

35. ENDOCRINE PROFILE OF AN OVARIAN ANDROBLASTOMA.

Munetsura M, Nakamura T, Matsuura K, Maeyama M, Iwamasa T (c/o Maeyama) Dept. Obstetrics and Gynecology, Kumamoto Univ. Medical Sch., Kumamoto 860, Japan
Obstet Gynecol; 59(6,Suppl):100S-104S 1982

The endocrine profile of a 16-yr-old girl with an androblastoma of the left ovary is presented. Calculated ratios of steroid hormones between the intraoperative peripheral vein blood, the left ovarian vein blood, and the left ovarian tumor fluid were progesterone, 1:10.2:39.5; 17-hydroxyprogesterone 1:18.7:64.7; dehydroepiandrosterone (DHEA), 1:10.4:35.6; androstenedione (A), 1:24.4:92.3; testosterone (T), 1:18.6:69.2; and estradiol (E2), 1:11.0.26.3. The peripheral levels of hormones before left salpingo-oophorectom were T, 7.5 ng/ml; DHEA, 19.9 ng/ml; A, 12.3 ng/ml; and cortisol, 11.4 ug/dl. Corresponding levels at 14 days after surgery were 0.75 ng/ml; 5.84 ng/ml; 1.94 ng/ml; and 15.6 ug/dl, respectively. Preoperatively, an elevated basal level of luteinizing hormone (LH) and a normal basal level of follicle-stimulating hormone (FSH) (high LH:FSH ratio) were found. These data suggest that (1) androgens from the androblastoma are responsible for virilization despite aromatizing enzyme activities within normal limits, and (2) both the delta5 and delta4 pathways are involved in the biosynthesis of androgens, with that of delta5 being predominant. (Author abstract) (12 Refs)

36. SURGICAL TREATMENT OF MESENCHYMAL AND SEXUAL CORD TUMORS.

Legros R
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Gynecologie; 33(1/2):31-36 1982

The surgical treatment of mesenchymal and sexual cord tumors of the ovary are discussed in connection with the treatment of 32 patients seen with such tumors in a group of 492 patients with ovarian tumors treated during a 20-yr period. The extent of surgery is dependent on the patient's age, general condition, and the benign or malignant nature of the tumor, which can most often be determined only during surgery. The 32 patients included 11 with fibromas, 16 with thecomas, 3 with granulosa-cell tumors and 1 each with granulosa-theca cell tumor and Leysig's-cell tumor. The tumors were bilateral in 5/32 patients, had diameters exceeding 5 cm in 13, and were associated with other pathological conditions in 23 (including ovarian dystrophy in 6, cystadenoma in 4, Brenner's tumor in 2, vascular anomalies in 10 and caseous abscess associated with tubal tuberculosis in 1). Twenty-four patients had benign tumors, 2 malignant tumors (thecoma and granulosa-cell tumor, respectively), and 6 (2/6 with fibromas and 4/6 with thecomas) had benign tumors associated with endometrial cancer. Ascites was found in 3 patients, endometriosis in 5, adhesion in 14, pregnancy (associated with chorioepithelioma in 1) in 3. Surgery consisted of total hysterectomy with adnexectomy in 15 patients, subtotal hysterectomy with adnexectomy in 2, extended hysterectomy in 4, ovariectomy in 6, tumorectomy in 3, exploratory surgery in 1 and surgery for ovarian cancer in 1. (no Refs) (In FRE)

37. HEXAMETHYLMELAMINE AND CISPLATIN IN ADVANCED OVARIAN CANCER AFTER FAILURE OF ALKYLATING-AGENT THERAPY.

Vogl SE, Pagano M, Davis TE, Einhorn N, Tunca JC, Kaplan BH, Arseneau JC
Albert Einstein Coll. Medicine Yeshiva Univ., 1300 Morris Park Ave., Bronx, NY, 10461
Cancer Treat Rep; 66(6):1285-1290 1982

Thirty-eight women with advanced ovarian cancer resistant to alkylating-agent chemotherapy were treated with a combination of hexamethylmelamine and cisplatin. Hematologic toxicity was severe or life-threatening in 7 of 13 patients treated with cisplatin at a dose of 100 mg/m2 but was acceptable in 25 patients treated at 75 mg/m2. Thirty-four percent of the combined group developed peripheral neuropathy and only 8% of those treated at 75 mg/m2 developed transient azotemia. Nine complete responses and 12 partial remissions were noted among 38 patients treated, with no obvious advantage for the higher dose of cisplatin. The median duration of remission was 8 months and the overall median survival was 9 months. The response rate of 55% is approximately twice that reported with either agent given alone in similar patient populations and is equal to or better than that reported for more complicated regimens containing these drugs together with other, less active drugs. (Author abstract) (24 Refs)

38. HIGH-DOSE MEDROXYPROGESTERONE ACETATE FOR THE TREATMENT OF ADVANCED OVARIAN CARCINOMA.

Trope C, Johnsson JE, Sigurdsson K, Simonsen E
Gynecologic Section, Dept. Oncology, Univ. Hosp., S-221 85 Lund, Sweden
Cancer Treat Rep; 66(6):1441-1443 1982

Effects of high-dose medroxyprogesterone acetate (MPA) were studied in 25 patients (43-81 yr old, median 61 yr) with recurrent, advanced (7 patients Stage III, 18 Stage IV) and chemotherapy-resistant ovarian carcinoma, with measurable or evaluable lesions. MPA was given im 500 mg/day for 3 wk, followed by 500 mg once a wk for at least 2 mo. Patients with an objective response or stable disease continued treatment with 500 mg every wk until disease progression. One patient achieved partial response (duration, 3+ mo; survival 4+ mo); 9 had stable disease (median duration, 5.5+ mo; median survival, 6.5 mo); and 15 had progressive disease (median survival, 3

mc). The objective response occurred in a 73-yr-old woman with undifferentiated carcinoma Stage IV. The patient had a greater than 50% reduction of central pelvic mass and inguinal nodes. Nine (36%) of the 25 patients increased their Karnofsky index by an av of 20 points. During therapy, no changes in blood counts or serum levels of creatinine, bilirubin, alkaline phosphatase, and fasting blood sugar were observed. More severe complications such as deep vein thrombosis were observed in two patients, but both had large pelvic tumors and had possibly developed thrombosis. The overall response rate was 4%. Since most of the epithelial ovarian carcinoma cell types were included in the study, results indicated that objective responses may be obtained only in a minority of patients with ovarian carcinoma resistant to cytostatic drugs. (5 Refs)

39. A CONTROLLED CLINICAL TRIAL IN ADVANCED OVARIAN CANCER.

Adams M, Johansen KA, James KW, Rocker I
Dept. Radiotherapy and Oncology, Velindre Hosp., Cardiff, Wales
Clin Radiol; 33(2):161-163 1982

Thirty-eight patients with an advanced ovarian cancer (FIGO Stage III and IV) were randomly allocated to treatment, either with melphalan (M) or a combination of adriamycin, 5-fluorouracil and cyclophosphamide (CAF) to determine the effect on survival. Actuarial survival of the two treatment groups was the same but the combination was more toxic. (Author abstract) (14 Refs)

40. TAMOXIFEN THERAPY FOR ADVANCED OVARIAN CANCER.

Schwartz PE, Keating G, MacLusky N, Naftolin F, Eisenfeld A
Dept. Obstetrics and Gynecology, Yale Univ. Sch. Medicine, 333 Cedar St., P.O. Box 3333, New Haven, CT, 06510
Obstet Gynecol; 59(5):583-588 1982

Thirteen patients with rapidly advancing recurrent epithelial ovarian cancers, in whom chemotherapy and, in some cases, radiation therapy failed, were treated with the estrogen antagonist tamoxifen. The presence of cytosol estrogen receptors, which have recently been identified in ovarian cancer specimens, was determined in the tumor from each patient prior to tamoxifen treatment. No complete responses were observed. One patient had a partial response and 4 patients had prolonged stabilization of disease. All patients with stabilized disease had estrogen receptor levels that were borderline or high. Eight patients demonstrated no response to oral tamoxifen therapy, but 5 of these had partial small bowel obstruction secondary to advanced recurrent cancer. As tamoxifen in this preliminary study may have stabilized rapidly advancing recurrent ovarian cancer, its role in the primary treatment of ovarian cancer in combination with cytotoxic chemotherapy should be considered. (Author abstract) (23 Refs)

41. BRENNER'S TUMOR OF THE OVARY, SYNOPSIS OF CLINICAL DATA AND HISTOLOGICAL FINDINGS.

Kostal M, Andrys J, Kopecny J
Gynek.-porod. klinika, LF KU, 500 36 Hradec Kralove, Czechoslovakia
Cesk Gynekol; 47(4):279-283 1982

Brenner's tumors of the ovary were diagnosed in 14 patients (49-78 yr old) during the period 1966-1981. There was only one nullipara among the 14 patients, the other 13 had had 1-7 childbirths. Twelve of the 14 patients were in menopause for 0.5-28 yr. Twelve of the 14 patients had symptoms, including mostly obstipation, metrorrhagia, and spotting. Brenner's tumor coinciding with adenocarcinoma of the uterine body was found in one patient, bilateral Brenner's tumor in another. Brenner's tumors were solid cystic in 4/14 patients, solid in 10. Treatment consisted of surgery in all cases: abdominal hysterectomy was performed in 5/14 patients, vaginal hysterectomy in 2/14, supracervical amputation in 1/14 and adnexectomy in 6/14. Hysterectomy and amputation were complemented by adnexectomy in all eight patients. No postoperative complications were observed. The possible risk of malignant transformation of Brenner's tumor and long-term estrogen stimulation of the target tissue by the tumor are emphasized. (11 Refs) (In CZE)

42. PRIMARY ADENOCARCINOMA OF THE FALLOPIAN TUBE.

Roberts JA, Lifshitz S
Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Univ. Iowa Hosp. and Clinics, Iowa City, IA, 52240
Gynecol Oncol; 13(3):301-308 1982

Primary carcinoma of the Fallopian tube is the rarest of all gynecologic malignancies. The experience obtained in treating this disease at the University of Iowa Hospitals and Clinics is reviewed. This information, combined with that of the recent literature, has been incorporated into life-table survival curves to show (1) decreasing 5-yr survival with increasing stage, (2) little mortality from this disease after 3 yr except in Stage II, and (3) no apparent difference in survival when the surgical treatment of Stages I and II is combined with either pelvic radiation or intraperitoneal radioisotopes. (Author abstract) (15 Refs)

43. PELVIC AND OVARIAN EXTRAMEDULLARY LEUKEMIC RELAPSE IN YOUNG GIRLS. A REPORT OF FOUR CASES AND REVIEW OF THE LITERATURE.

Cecalupo AJ, Frankel LS, Sullivan MP
(c/o Frankel) Dept. Pediatrics, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Cancer; 50(3):587-593 1982

Currently attention is focused on the testicle as a site of leukemic relapse. Leukemic involvement of the ovary has been described in several autopsy series with an incidence of 11-50% in patients with bone marrow relapse, but has rarely been reported during the clinical course of leukemia. In this report, four girls with childhood acute lymphocytic leukemia (ALL) who relapsed with a pelvic mass are presented. Three had marked ovarian infiltrates and the fourth had a presacral mass without ovarian disease. Involvement was also present in abdominal and pelvic lymph nodes, mesentery, omentum, and serosal surfaces. Two patients had infiltrates of the fallopian tubes and one had uterine involvement. Two patients had central nervous system disease and one patient had renal involvement at the time of relapse. Relapse occurred late in the course of disease. All patients had been in complete continuous remission prior to relapse. Retreatment was instituted in all patients and follow-up ranges from 18-135 mo from the time of pelvic relapse. All patients have maintained continuous bone marrow remission from the time of initial diagnosis, and one patient died 18 mo after ovarian relapse with significant extramedullary disease but no marrow involvement. This represents the first series of pelvic extramedullary leukemic relapse in females, an area of involvement that may be encountered more frequently in the future. (Author abstract) (42 Refs)

44. LOW SERUM IGA IN A FAMILIAL OVARIAN CANCER AGGREGATE.

Schwalke GS, Lynch HT, Lynch JF, Fain PR, Chaperon EA
Dept. Medical Microbiology, Creighton Univ. Sch. Medicine, 2500 California St., Omaha, NE, 68178
Cancer Genet Cytogenet; 6(3):231-236 1982

Low serum IgA levels were found to segregate in a sufficient number of individuals from a familial ovarian carcinoma aggregate to suggest that this may be a genetically determined immune defect etiologically integral to cancer susceptibility in this family. The putative role of IgA in pathogenesis remains elusive. Cancer-prone families should be thoroughly investigated for further elucidation of these phenomena. (Author abstract) (24 Refs)

45. SURVEILLANCE AND MANAGEMENT OF PATIENTS AT HIGH GENETIC RISK FOR OVARIAN CARCINOMA.

Lynch HT, Albano WA, Lynch JF, Lynch PM, Campbell A
Dept. Preventive Medicine, Creighton Univ. Sch. Medicine, 2500 California St., Omaha, NE, 68178
Obstet Gynecol; 59(5):589-596 1982

The present study is concerned with surveillance/management programs for hereditary ovarian cancer syndromes. These syndromes lack distinguishing premonitory physical signs or biomarkers; therefore, in these genotypic settings, ovarian cancer risk must be assessed by analysis of the patient's pedigree. The authors describe 10 families showing a hereditary proclivity to ovarian carcinoma and/or associated cancer(s) in accord with their respective cancer-prone genotypes. Cancer education, genetic counseling, and surveillance should be instituted early. In addition to bimanual pelvic examination, ultrasound should be tested for its possible efficacy as a screening technique. The option of prophylactic bilateral oophorectomy and hysterectomy is thoroughly discussed with highly selected candidates. The authors believe that the aggressive management approach proposed for ovarian carcinoma is warranted for high-risk members of cance-prone families, wherein the risk for ovarian cancer may approach 50%. (Author abstract) (18 Refs)

46. OVARIAN CANCER AND TALC. A CASE-CONTROL STUDY.

Cramer DW, Welch WR, Scully RE, Wojciechowski CA
Dept. Obstetrics and Gynecology, Brigham and Women's Hosp., Boston, MA, 02115
Cancer; 50(2):372-376 1982

Opportunities for genital exposure to talc were assessed in 215 white females with epithelial ovarian cancers and in 215 control women from the general population matched by age, race, and residence. Ninety-two (42.8%) cases regularly used talc either as a dusting powder on the perineum or on sanitary napkins compared with 61 (28.4%) controls. Adjusted for parity and menopausal status, this difference yielded a relative risk of 1.92 (p less than 0.003) for ovarian cancer associated with these practices. Women who had regularly engaged in both practices had an adjusted relative risk of 3.28 (p less than 0.001) compared to women with neither exposure. This provides some support for an association between talc and ovarian cancer hypothesized because of the similarity of ovarian cancer to mesotheliomas and the chemical relation of talc to asbestos, a known cause of mesotheliomas. The authors also investigated opportunities for potential talc exposure from rubber products such as condoms or diaphragms or from pelvic surgery. No significant differences were noted between cases and controls in these exposures, although the intensity of talc exposure from these sources was likely affected by variables not assessed in this study. (Author abstract) (24 Refs)

TROPHOBLASTIC DISEASE

47. PATTERNS AND PITFALLS IN THE ULTRASONIC DIAGNOSIS OF MOLAR PREGNANCY.

Lingard DA
Kingway Diagnostic Center, 729 Pittwater Road, Dee Why, N.S.W. 2099, Australia
Australas Radiol; 26(1):73-78 1982

A retrospective review of 7,800 obstetric ultrasound examinations is presented. It revealed 30 examinations, representing 26 different pregnancies, in which trophoblastic disease was suspected. There were 17 true positive (13 pregnancies), 13 false positive, and two false negative examinations indicating a greater uncertainty in the ultrasonic diagnosis of trophoblastic disease than is generally thought. The most commonly encountered patterns are an enlarged uterus filled with what looks like a porous placenta, enhanced through sound transmission, and large irregularly shaped cystic spaces. The entities most likely to cause confusion include multiple fibroids (with or without intrauterine conceptual products), missed or incomplete abortions, and blighted ova. Less common causes of misdiagnosis such as a Braxton-Hicks contraction, and choriodecidual sinuses with prominent draining veins are also described. (Author abstract) (8 Refs)

48. THE CLINICOPATHOLOGIC PROFILE OF THE PARTIAL HYDATIDIFORM MOLE.

Szulman AE, Surti U
Dept. Pathology, Magee-Womens Hosp., Pittsburgh, PA, 15213
Obstet Gynecol; 59(5):597-602 1982

Having delineated the complete and the partial hydatidiform moles as 2 separate entities on the basis of morphology and cytogenetics, the authors studied 201 molar pregnancies at the Magee-Womens Hospital in an attempt to characterize the clinicopathologic profile of the partial mole syndrome. This was done mainly by comparison and contrast with the established and more familiar syndrome of the classic complete mole. The partial mole syndrome displays most of the pathologic and clinical features of the classic mole and seems to represent a milder, dilute version of the latter. This applies to placental morphology, to the fate of the embryo/fetus, and to human chorionic gonadotropin (hCG) levels as well as to the incidence and severity of clinically persistent trophoblastic disease. Preeclampsia can be equally severe in both syndromes, but tends to occur later in patients with partial mole. No metastatic disease was encountered in association with partial moles and no case of overt choriocarcinoma has yet been described. The occurrence of trophoblastic disease (as determined by postoperative hCG titers) following partial moles requires further inquiry, including study of the pathology of the underlying lesion(s), which remain virtually unexplored. (Author abstract) (22 Refs)

49. SERUM SP1 AND HCGBETA-SUBUNIT (HCGBETA) LEVELS IN CHORIOCARCINOMA, INVASIVE MOLE, AND HYDATIDIFORM MOLE - CLINICAL SIGNIFICANCE OF SP1/HCGBETA RATIO.

Sakuragi N

Dept. Obstetrics and Gynecology, Sch. Medicine, Hokkaido Univ., Sapporo, Japan

Gynecol Oncol; 13(3):393-398 1982

Serum Sp1 (pregnancy-specific beta1 glycoprotein) levels in patients with choriocarcinoma, invasive mole, and hydatidiform mole were radioimmunoassayed and compared with simultaneously measured serum hCGbeta-subunit (hCGbeta) levels in order to evaluate the clinical significance of SP1 determination. Serum SP1 levels at the time of admission ranged from 6.4 to 1,660 ng/ml in choriocarcinoma patients, 16.3 to 540 ng/ml in invasive mole, and 720 to 58,000 ng/ml in hydatidiform mole. Sp1/hCGbeta ratios were under 1.0 in choriocarcinoma (0.3 +-0.2, mean +- SD), over 1.0 in hydatidiform mole (10.9 +-8.3), and intermediate in invasive mole (1.5 +-0.3). In normal pregnancy, the ratio increases as pregnancy progresses, that is, from 15.25 in 7-wk gestation to 14,090.90 in 40-wk gestation. The mean SP1/hCGbeta ratio differs significantly among choriocarcinoma, invasive mole, and hydatidiform mole. SP1/hCGbeta ratio is likely to represent the degree of differentiation of trophoblastic cells. The SP1/hCGbeta ratio may be useful in differentiating between choriocarcinoma and invasive mole. (Author abstract) (4 Refs)

50. CIRCULATING IMMUNE COMPLEX LEVELS IN PATIENTS WITH GESTATIONAL TROPHOBLASTIC NEOPLASIA.

Rayner AA, Berkowitz R, Steele G, Schur PH, Rodrick ML, Goldstein DP, Hartz PJ, Wilson RE, Zamcheck N, Munroe AE

(c/o Steele) Dept. Surgery, Brigham and Women's Hosp., Harvard Medical Sch., 75 Francis St., Boston, MA, 02115

JNCI; 69(1):23-26 1982

The clinical course, human chorionic gonadotropin (HCG) levels, and serial circulating immune complex (CIC) levels in 21 patients with gestational trophoblastic neoplasia (GTN) were correlated for the evaluation of the relationship between CIC levels and trophoblastic tumor burden. CIC levels were normal in 18 of 21 patients at the time of presentation, and 2 of the 3 patients who presented with elevated CIC levels had significant comorbid disease (toxemia and hepatitis). Nine patients were followed into gonadotropin remission, and all nine developed an increase in CIC levels at the time of remission. It was concluded that CIC, at least as measured by two antigen-nonspecific techniques, is generally not elevated at initial presentation in the patient with GTN; this lack of an elevation is probably due to marked tumor antigen excess. Thus the in vivo importance of CIC as a 'blocker' of host antitumor response at this stage is doubtful. After effective treatment as HCG levels return to normal, the demonstrated elevation in serial levels of CIC may reflect a return of adequate host immune response at a time of minimal tumor burden. (Author abstract) (16 Refs)

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VULVAR TUMORS

1. VULVAR MELANOMA: A MICROSTAGING STUDY.

Phillips GL, Twiggs LB, Okagaki T
Div. Gynecologic Oncology, Div. Gynecologic Pathology, Univ. Minnesota Hosp., Minneapolis, MN, 55455
Gynecol Oncol; 14(1):80-88 1982

A retrospective review and a histopathologic analysis were conducted of 18 cases of malignant melanoma of the vulvar. FIGO staging did not correlate well with survival. Microstaging, as defined by the combination of Clark's level and Breslow's depth of invasion, was the most significant prognostic factor. (Author abstract) (16 Refs)

2. MULTIPLE SQUAMOUS-CELL CARCINOMAS IN FANCONI'S ANEMIA.

Kennedy AW, Hart WR
(c/o Hart) Dept. Pathology, Cleveland Clinic Foundation, 9500 Elucid Ave., Cleveland, OH, 44106
Cancer; 50(4):811-814 1982

Fanconi's anemia is one of the chromosome instability syndromes that may predispose to the development of cancer. A 20-yr-old woman is reported in whom microinvasive squamous-cell carcinomas of the vulva and tongue developed sequentially. The clinicopathologic findings of 13 other cases of Fanconi's anemia associated with squamous-cell carcinomas are reviewed. Anogenital and oral mucosal surfaces appear to be sites of predilection for these cancers. Patients with relatively mild bone marrow problems or the preanemic phase of the illness who are able to survive several decades appear to be at greatest risk for the development of squamous-cell carcinoma. (Author abstract) (41 Refs)

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3. EXPRESSION OF HERPES SIMPLEX VIRUS TYPE 2 ANTIGENS IN PREMALIGNANT AND MALIGNANT HUMAN VULVAR CELLS.

Cabral GA, Marciano-Cabral F, Fry D, Lumpkin CK, Mercer L, Goplerud D

Dept. Microbiology, Medical Coll. Virginia, Virginia Commonwealth Univ., Box 678-MCV Station, Richmond, VA, 23298

Am J Obstet Gynecol; 143(6):611-619 1982

Vulvar biopsies and explants from patients with vulvitis, hyperkeratosis, condyloma acuminatum, severe dysplasia, and squamous cell carcinoma were screened for herpes simplex virus Type 2 (HSV-2) antigens. Immunoperoxidase staining for VP143, an early nonstructural polypeptide of HSV-2, was identified within three biopsies exhibiting severe dysplasia, three of seven with carcinoma in situ, and one of three with invasive squamous cell carcinoma. Similar staining for VP143 was observed in derived explants. Staining for VP119, the major envelope glycoproteins of HSV-2, was identified within tissues which were positive for VP143. Both proteins were expressed in the absence of staining for virus capsid proteins, detection of virus structures by electron microscopy, and isolation of infectious virus by co-cultivation, indicating that only a fragment of the virus genome was expressed. Neither VP143 nor VP119 was identified in biopsies exhibiting vulvitis, hyperkeratosis, or condyloma acuminatum. These data indicate a close relationship between HSV-2 and vulvar neoplasia. (Author abstract) (19 Refs)

VAGINAL TUMORS

4. NEOPLASMS OF THE VAGINA FOLLOWING CERVICAL CARCINOMA.

Choo YC, Anderson DG

Div. Gynecologic Oncology, Dept. Obstretrics and Gynecology, Univ. Michigan Hosp., Ann Arbor, MI, 48109

Gynecol Oncol; 14(1):125-132 1982

Neoplasm in the vagina which occurs following treatment of cervical carcinoma could represent a separate primary neoplasm, a 'field' response to a common carcinogen, or be due to neoplastic transformation of tissue from previous radiation treatment. Fifty patients with a second neoplasm in the vagina were identified: 17 following total hysterectomy for carcinoma in situ of cervix; 4 following radical hysterectomy; and 29 following radiotherapy for invasive cervical carcinoma. Their clinical features, diagnosis, and treatment modalities are presented. Since vaginal neoplasm may occur long after treatment of the initial cervical carcinoma especially after previous radiotherapy, life-long follow-up of all patients with cervical carcinoma is mandatory. (Author abstract) (28 Refs)

CERVICAL AND UTERINE TUMORS

5. CERVICAL INTRAEPITHELIAL NEOPLASIA AND 'WARTY' ATYPIA: A STUDY OF COLPOSCOPIC, HISTOLOGICAL AND CYTOLOGICAL CHARACTERISTICS.

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Br J Obstet Gynaecol; 89(7):571-577 1982

A consecutive series of 168 patients referred to the colposcopy clinic because of abnormal cervical cytology were examined for three groups of features. Colposcopic features included indefinite and finger-like lesion outline, satellite lesions, open or non-open mosaic, loop capillaries, and overall impression of non-condylomatous wart virus infection (NCWVI). Histological features included koilocytosis (KO), double nucleation (DN), dyskeratosis, hyperkeratosis, dyskaryosis, frequent mitoses, acanthosis, prominent rete pegs, epithelial pearls and overall impression of NCWVI. Cytological features included KO, DN and dyskeratosis. A group of patients exhibited a cluster of histological features related to possible human papilloma virus infection of the cervical epithelium, particularly KO, DN and dyskeratosis. Two colposcopic findings were significantly increased in these patients, 'finger-like' lesion outline and impression of warty change. Cytological changes previously related to warty lesions were not of common occurrence. Cervical intraepithelial neoplasia was rare in women in whom less than 10 yr had elapsed since first intercourse, whereas lesions showing changes suggestive of a warty etiology were evenly distributed between patients at more and less than 10 yr from first intercourse. (14 Refs)

6. MIXED MULLERIAN TUMORS OF THE UTERUS: CLINICAL AND PATHOLOGIC CORRELATIONS.

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Int J Gynaecol Obstet; 20(3):237-243 1982

Cases of 61 women (39-90 yr old; mean age 63.7 yr) with mixed Mullerian tumors of the uterus are reviewed. Clinical manifestations of the disease included vaginal bleeding (53) and combination of vaginal discharge, pain, wt loss, weakness, and anorexia (8). Preoperative staging showed that 37 patients were in Stage I, 3 Stage II, 17 Stage III, and 4 Stage IV. Fifteen patients had a history of other malignancies (10 cervical carcinoma, 1 bladder carcinoma, 1 cervical and rectal carcinoma, 2 breast cancer, and 1 multiple myeloma). Eleven patients had a history of previous radiotherapy. Of 61 patients, 52 were subjected to radical surgery and/or radiotherapy, and 9 received palliative treatment. Radical surgery included total abdominal hysterectomy, bilateral salpingo-oophorectomy, Wertheim hysterectomy, bilateral pelvic lymphadenectomy, total pelvic exenteration, or subtotal abdominal hysterectomy. Histological examination of tumor specimens showed heterologous elements in 17 patients, while 44 were classified as homologous mixed Mullerian tumors. The patients were followed-up for 3 mo to 10 yr after initial diagnosis and treatment. The 2-and 5-yr survival rates were 46.8% and 41.1%, respectively. Prognosis was related to the extent of tumor invasion, the amount of residual tumor, and the previous history of pelvic irradiation. (22 Refs)

7. HISTOLOGIC VARIANTS OF CERVICAL INVOLVEMENT BY ENDOMETRIAL CARCINOMA.

Kadar NR, Kohorn EI, Wolsi VA, Kapp DS
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Obstet Gynecol; 59(1):85-92 1982

Examination of histologic material from 54 patients with endometrial carcinoma, in whom the pretreatment fractional curettage showed adenocarcinoma in the endocervical specimen, demonstrated four main patterns. These were designated as tumor separate from endocervical tissue (13 patients), true Stage II (23 patients), tumor in stroma (12 patients), and tumor only (6 patients). Patients with tumor separate from endocervical tissue had a better survival rate (expressed as survival to first recurrence) than did patients in the other three groups, and this difference was statistically significant. No statistically significant difference between the survival of patients in the true Stage II, tumor in stroma, and tumor only groups could be demonstrated. It is therefore suggested that the treatment protocol used for these three groups of patients be similar. Among the true Stage II group, only three patients had superficial endocervical involvement, whereas 15 had stromal involvement without surface tumor. Therefore, spread to the cervix in endometrial carcinoma appears to be more frequent by tissue spaces or lymphatic channels than by contiguous surface extension. (Author abstract) (11 Refs)

8. GLASSY CELL CARCINOMA OF THE CERVIX.

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Obstet Gynecol; 60(2):219-224 1982

Of the 389 cases of primary adenocarcinoma of the cervix in the Armed Forces Institute of Pathology files, only 9 (2%) demonstrated features of glassy cell carcinoma in one third or more of the tumor. Histologically, glassy cell carcinomas were associated with admixed areas of mucinous adenocarcinoma in five instances, and four of the nine neoplasms contained glandular differentiation by glassy cells. Squamous differentiation occurred in four of the nine cases, and intracellular mucin was present in seven of the eight glassy cell carcinomas stained for it. Even in the single example without demonstrable mucin production gland formation by the tumor cells was evident. Although the cells have a characteristic appearance, it is unclear if glassy cell carcinoma is a meaningful entity. The need for its separate designation in the classification of cervical carcinoma is questionable. If glassy cell carcinoma exists, examples probably will be found within categories of nonkeratinizing large cell carcinoma and undifferentiated carcinoma. (Author abstract) (9 Refs)

9. DIAGNOSTIC MARKER FEATURES IN DYSPLASTIC CELLS FROM THE UTERINE CERVIX.

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Acta Cytol (Baltimore); 26(4):475-483 1982

A study of dysplatic cells, visually classified as nonkeratinizing (DYSN), keratinizing (DYSK) or severely dysplastic from an area of metaplasia (DYSM), demonstrated statistically significant differences between the same type of cell depending on the diagnostic category of the patient in which it originated: cases with moderate dysplasia (MOD), severe dysplasia/carcinoma in situ (CSD) or invasive carcinoma (INV). The results suggest that the cell types should include an indication of their origin, that, eg, DYSN is an insufficient designation and that such cells should be denoted as DYSN-MOD, DYSN-CSD or DYSN-INV; this has major implications for the collection of cell image data bases for quantitative cytology as well as for the effort to characterize patients' cytologic samples by 'cytodiagnostic profiles'. The results also indicate that the samples as a whole contain many clues to patient diagnosis; examples are given of diagnostic profiles and the related computergraphic displays for different patient categories. (Author abstract) (9 Refs)

10. STROMAL METACHROMASIA: A MARKER FOR AREAS OF INFILTRATING TUMOR GROWTH?

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Histopathology; 6(4):423-428 1982

The stromal reaction in the zone of host/tumor interaction in 38 cases of infiltrative carcinoma of the uterine cervix was compared to that at the base of the epithelial layer in 35 cases of carcinoma in situ at the same site. Sections were cut from selected blocks and stained with toluidine blue at pH 4. A pilot study revealed areas of metachromasia at the zone of host/tumor interaction in 7/10 of the infiltrative lesions, but in none of the carcinoma in situ specimens. The areas of metachromasia had stromal cells with large, ill-defined edges, with a suggestion of a parallel fibrillar structure in places. Cell nuclei were large and vesicular, often with a lobulated nuclear membrane, and characteristic 'bent' oval shape. In the main series, 23/38 infiltrative cancer specimens showed stromal metachromasia, with morphological changes as found in the pilot study. Only one of the 35 carcinoma in situ lesions exhibited weak metachromasia at the zone of host/tumor interaction; this may have been due to staining too close to edge of the section. The absence of stromal metachromasia in in-situ lesions in which cells fulfill the morphological criteria for malignancy indicates that metachromasia is not an aid to the diagnosis of malignancy. It may serve as a marker for areas of active stroma formation and thus give an indication of the physiological status of the tumor in a given area. (8 Refs)

11. DESMOSOMES AND GAP-JUNCTIONS IN VARIOUS EPIDERMOID PRENEOPLASTIC AND NEOPLASTIC LESIONS OF THE CERVIX UTERI.

Schindler AM, Amaudruz MA, Kocher O, Riotton G, Gabbiani G
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Acta Cytol (Baltimore); 26(4):466-470 1982

The distribution of desmosomes and of gap-junctions was studied by morphometric means, at the electron microscopic level, in the following lesions of the uterine cervix: metaplasia, moderate and severe dysplasia, carcinoma in situ and invasive epidermoid carcinoma. The results were compared with normal exocervical epithelium. The proportion of the cell surface occupied by gap-junctions was decreased in all lesions; gap-junctions were statistically absent from moderate dysplasia and more advanced lesions. The number of desmosomes decreased gradually from metaplasia to invasive carcinoma, with each stage forming a discrete group. This gradual loss of intercellular structures with increasing degrees of malignancy might express dedifferentiation and could be associated with increasing cellular autonomy. (Author abstract) (8 Refs)

12. SCANNING ELECTRON MICROSCOPY OF NORMAL CELLS, DYSKARYOTIC CELLS AND MALIGNANT CELLS EXFOLIATED FROM THE UTERINE CERVIX.

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Acta Cytol (Baltimore); 26(4):457-465 1982

The same exfoliated benign, dyskaryotic and malignant cervical cells were observed by light microscopy and scanning electron microscopy in order to investigate the reflection of the course of malignancy in the surface ultrastructure. The surface ultrastructural features (microridges and microvilli) or normal squamous cells and metaplastic cells showed regularities, with an approximately even thickness, length and distribution of microvilli. In dyskaryotic cells of the superficial type, the microridge-like structure was retained, and some regularity of the microvilli remained. However, in dyskaryotic cells of the deep-layer type, the microvillous surface ultrastructure had a pronounced irregularity and diversity. In malignant cells, there was unevenness in the projections and in the thickness of the cytoplasm, and these cells presented, as a whole, a bizarre appearance. The surface ultrastructure of malignant cells thus reflected a strong atypia of the cytoplasm. (Author abstract) (6 Refs)

13. ESTRADIOL AND PROGESTIN RECEPTORS, 17-BETA-HYDROXYSTEROID-DEHYDROGENASE AND HISTOPATHOLOGIC GRADE IN ENDOMETRIAL CARCINOMA.

Ciuffi M, Savino L, Santini D, Buzzoni P, Scarselli G, Mazzei T
Clinica Ostetrica e Ginecologica, Universita, Viale Morgagni, 50100 Firenze, Italy
Tumori; 68(3):217-221 1982

The possible correlations between steroid receptor systems, 17-beta-hydroxysteroid-dehydrogenase (17-beta-HSD) and histopathologic examinations were investigated. The well-differentiated tumors showed higher steroid receptor and 17-beta-HSD values than undifferentiated carcinomas. The steroid receptors did not present a statistically significant correlation with 17-beta-HSD. Nevertheless, some neoplastic endometria (29%) show higher values of progestin receptors and 17-beta-HSD, with a progestin:estrogen receptor ratio greater than one. (Author abstract) (15 Refs)

14. ESTROGEN RECEPTORS IN HUMAN UTERINE ADENOCARCINOMA: CORRELATION WITH TISSUE DIFFERENTIATION, VAGINAL KARYOPYCNOTIC INDEX, AND EFFECT OF PROGESTOGEN OR ANTI-ESTROGEN TREATMENT.

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Gynecol Oncol; 14(1):33-39 1982

Estrogen receptor levels were measured in the cytosol of uterine adenocarcinomas obtained by endometrial biopsy in 37 postmenopausal women. The karycpycnotic index was determined individually by vaginal smear. It was considered estrogenic when superior to 5% (KI+). The histologic characteristics of the tumors were classified as well (D+) or poorly (D-) differentiated. The receptor level was highest in D+KI- tumors (103 +-19 (SEM) fmole/mg protein), intermediate in D+KI+ tumors (44 +-12), and lowest in D- tumors (25 +-10). During medroxyprogesterone acetate (MPA) treatment, the receptor level dropped rapidly in D+ tumors (from 87 +-14 to 16 +-5) and remained low in D- tumors (25 +-10 to 1 +-1). Tamoxifen (T) treatment also produced a reduction in the receptor levels: in D+ tumors to 1 +-1 and in D- tumors to 6 +-2. In conclusion, high receptor levels in cytosol of D+ tumors as well as the significant reduction under MPA or T treatment suggest the persistence in these tumors of hormonal regulatory mechanisms. Estrogenic impregnation of the patient should, however, be taken into account to differentiate between the hormone-sensitive D+KI+ tumors and the receptor-poor D- tumors. (Author abstract) (23 Refs)

15. CARCINOMAS OF THE CERVIX AND CORPUS UTERI IN HUMANS: STAGE-DEPENDENT BLOOD LEVELS OF SUBSTANCE(S) IMMUNOLOGICALLY CROSS-REACTIVE WITH INSULIN.

Pavelic K, Bolanca M, Vecek N, Pavelic J, Marotti T, Vuk-Pavlovic S (c/o Vuk-Pavlovic), Inst. Immunology, Rockefellerova 2, 41000 Zagreb, Croatia, Yugoslavia
JNCI; 68(6):891-894 1982

Inasmuch as the elevated levels of substance(s) immunologically cross-reactive with insulin (SICRI) in a diabetic woman with carcinoma of the corpus uteri decreased following the surgical removal of the uterus and ovaries 80 women with cervical carcinomas of various stages and 70 women with carcinomas of the corpus uteri of various stages were screened for the levels of SICRI and C-peptide. The levels of SICRI in the 2nd, 3rd, and 4th stages of the cancers were elevated (up to 6x above the normal levels of immunoreactive insulin) and stage-dependent. The levels of C-peptide, which are related to the insulin-secreting activity of pancreatic beta-cells, were normal and independent of the stage of cancer. (Author abstract) (19 Refs)

16. ESTRADIOL, ANDROSTENEDIONE, TESTOSTERONE, AND DEHYDROEPIANDROSTERONE SULFATE IN THE OVARIAN AND PERIPHERAL BLOOD OF POSTMENOPAUSAL PATIENTS WITH AND WITHOUT ENDOMETRIAL CANCER.

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Clinique Gynecologique, Pavillion L, Hopital Edouard Herriot, Place d'Arsonval, 69374 Lyon Cedex 2, France
Gynecol Oncol; 14(1):119-124 1982

Estradiol (E), androstenedione (A), testosterone (T), and dehydroepiandrosterone sulfate (DHEAS) were determined in the plasma taken from the ovarian and cubital vein in endometrial cancer patients and controls. All the cases and controls experienced their menopause more than 4 yr before the study. The patients were matched for wt and height. No difference was found for T, A, and DHEAS in the peripheral blood between cases and controls. Nevertheless a statistically significant difference was observed for T and A, higher in the cases than in the controls: 4.38 +-1.32 vs 1.38 vs 0.51, for T and 5.69 +-1.65 vs 2.57 +-0.12 for A. Estradiol was higher in peripheral and ovarian blood of cancer cases when compared with the controls but the difference is not statistically significant. (Author abstract) (11 Refs)

17. NATURAL KILLER LYMPHOCYTE FUNCTION IN CERVICAL CANCER PATIENTS.

Puley TA, Benczur M, Varga M
Dept. Gynecology and Obstetrics, Semmelweis Medical Univ., 1088 Budapest, Hungary
Neoplasma; 29(2):237-240 1982

Authors investigated the natural killer and antibody dependent cellular cytotoxicity functions of lymphocytes in cervical cancer patients. According to the results the natural killer function showed remarkable changes related to the extent and the course of the disease. On the contrary, radiation therapy did not influence this function. The antibody dependent cellular cytotoxicity function of the same lymphocytes did not show any alteration under circumstances mentioned above. (Author abstract) (10 Refs)

18. MORPHOMETRIC STUDY OF INTRAEPITHELIAL NEOPLASIA OF THE UTERINE CERVIX.

Abdul-Karim FW, Fu YS, Reagan JW, Wentz WB
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Obstet Gynecol; 60(2):210-214 1982

Treatment failure for intraepithelial neoplasia of the uterine cervix following electrocautery, cryosurgery, or carbon dioxide laser therapy is related primarily to incomplete eradication of the lesion. This may be due to the depth of crypt involvement, the linear extent, or the location of the abnormal epithelium. In view of this, the extent (depth and linear extent) and the location of cervical intraepithelial neoplasia (CIN) in 319 cervical cone specimens were analyzed. There is a significant correlation between the severity and the extent of the change. The mean depths for CIN I, II and III were 0.42 +-0.28, 0.93 +-0.71, and 1.35 +-1.15 mm, respectively. The mean linear extents for CIN I, II, and III were 4.10 +-2.84, 5.84 +-4.13, and 7.60 +-4.32 mm, respectively. To eradicate 99.7% of CIN III lesions, it is necessary to destroy the tissue up to 4.80 mm in depth and of sufficient linear extent. While most lesions (87.2%) involved the transformation zone, 9.7% were higher in the cervical canal and 3.1% were located in the ectocervix. Appropriate cytologic samples, endocervical curettage, and colposcopic examination should be employed in evaluating the CIN, and strict criteria should be followed in selecting the patients for conservative management. (Author abstract) (18 Refs)

19. PARAAORTIC LYMPH NODE EVALUATION IN STAGE I ENDOMETRIAL CARCINOMA.

Piver MS, Lele SB, Barlow JJ, Blumenson L
Dept. Gynecology and Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263
Obstet Gynecol; 59(1):97-100 1982

Of 41 women with FIGO Stage I endometrial adenocarcinoma who underwent staging paraaortic lymphadenectomy and paraaortic node biopsy, 6 (14.6%) had metastasis to the paraaortic lymph nodes. None of the 11 patients with Grade 1 carcinoma had paraaortic node metastasis; 13.6% of Grade 2 carcinomas and 37.5% of Grade 3 carcinomas were associated with paraaortic node metastasis. None of the eight patients with tumor limited to the endometrium had paraaortic metastasis, and only 4.5% of the patients with superficial myometrial invasion had metastasis to the paraaortic lymph nodes. However, this increased to 45.5% for tumors deeply invading the myometrium. Of the patients with paraaortic node metastasis, 83.3% had either Grade 3 tumors or deep myometrial invasion. Only one patient in the study with paraaortic node metastasis did not have either a Grade 3 carcinoma or a tumor deeply invading the myometrium. Because of the high incidence of paraaortic node metastasis with Grade 3 tumors or deep myometrial invasion, surgical staging by paraaortic lymphadenectomy or lymph node biopsy is recommended at the time of primary surgery for early endometrial adenocarcinoma. (Author abstract) (5 Refs)

20. THE USE OF EMBOLIZATION IN UTERINE TUMOURS.

Ziviello M, Maglione F, Russo S
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Excerpta Med Int Congr Ser; 575:117-119 1982

Experience with embolization in the treatment of severely hemorrhagic uterine tumors diagnosed in 12 patients (av 55 yr old) is reported. Eight of the patients had tumors in the body and four in the cervix of the uterus. Severe metrorrhagia which could not be controlled by standard methods was present in all patients. In 3/12 patients, embolization of the hypogastric arteries was performed followed by surgical operation 2, 4, and 5 days later, respectively. In 7/12 patients, the embolization was not followed by operation. Selective bilateral catheterization of the hypogastric arteries was performed in 9/12 patients, of only one artery in 1, and selective bilateral catheterization in 1. Embolization was performed with Gelofoam and IBC. Preoperative embolization arrested bleeding immediately. The operation was always easier and shorter in duration as compared with similar operations where the hypogastric arteries were ligated. Palliative embolization was performed in five patients who survived and two who died 1 mo and 2 yr, respectively, after embolization. Recurrence of bleeding occurred at intervals of 14 days to 1 yr. One patient died after 1 mo from hemorrhage and an other died from carcinomatosis and cachexia after 1 yr. Complications were slight and consisted of pain in the buttocks (8 patients) and of mild and transient pyrexia (10 patients). (12 Refs)

21. SURGICAL MANAGEMENT OF ENDOMETRIAL CARCINOMA.

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Clin Obstet Gynecol; 25(1):81-92 1982

Staging, surgery for Stages I-IV and recurrent endometrial carcinoma (EC), and management of EC diagnosed postoperatively are discussed. Procedures employed in determining the apparent extent of disease at diagnosis and assigning the case to a category in an official staging system are the connotations of staging. Accurate surgical-pathological data should be incorporated into the EC staging system. Operation prior to administration of irradiation in all Stage I and occult Stage II EC avoids the delay in removing the primary lesion and improves the data base for treatment planning. Preoperative irradiation is, however, a common practice, and it is good treatment provided that certain special situations requiring surgery first are honored. Operative tumor spread, radiation-hysterectomy interval, abdominal, vaginal, and radical hysterectomy, and receptor analysis are discussed. Patients with Stage II EC should be operated and then irradiated. Patients who have Stage III EC by virtue of vaginal or parametrial extension or both and who experience complete regression of the tumor in these areas after radiation therapy should undergo exploratory laparotomy for the purposes of surgical staging. Approx half of the

patients with vaginal vault recurrences following surgery alone have disease that will not be cured by irradiation or excision and irradiation. For this reason, exploratory laparotomy is carried out to assess the true extent of disease by peritoneal cytology and evaluation of the aortic, common, and pelvic nodes, the omentum, and the liver. Recommendations for postoperative treatment are based on the known risk for extrauterine and extrapelvic disease related to histologic grade and myometrial penetration. (37 Refs)

22. POST-OPERATIVE RADIATION THERAPY IN CERVICAL CARCINOMA (MEETING ABSTRACT).

Perkins PL, Chu AM, Jose B, Achino E
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Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Thirty-six patients found to have incidental cervical carcinoma on hysterectomy for benign disease were treated post-operatively using whole pelvis irradiation. In 5 of these 36 patients, the tumor extended to the margins of resection. Two patients had adenocarcinoma, the remaining 34 were squamous cell carcinomas. Megavoltage anterior/posterior whole pelvis irradiation to at least 4500 rads was used in 32 of the 36 patients. A significant proportion received additional treatment to the vaginal apex either by Manchester ovoids (12) or by 250 KV trans-vaginal cone (13). Length of followup ranged from 3 years to 33 years with a median and modal followup of 6 years. The results of this treatment were not equal to those of standard radiotherapy techniques in early stages cervical carcinoma. The use of additional vaginal radiation did not seem to improve results. Eleven of these 36 patients had recurrent disease. In 5 of these, there was documented local recurrence, with a median time to recurrence of 33 months. None of the patients with recurrences were salvaged. The number of complications was high -9 of 36. But the majority of these complications were mild and 5 of 9 patients also had locally recurrent disease. There was one small bowel complication, an ileo-vaginal fistula - in a patient who had a vaginal recurrence. There were no cases of small bowel obstruction. Two patients had second primaries in the vagina at 33 and 19 years after treatment. (no Refs)

23. UTERINE PERFORATION DURING INTRACAVITARY APPLICATION - IT'S PROGNOSTIC SIGNIFICANCE IN CARCINOMA OF THE CERVIX (MEETING ABSTRACT).

Kim RY, Brascho DJ
Department of Radiation Oncology, University of Alabama in Birmingham, Birmingham, AL
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

We reviewed all cases of uterine perforation during intracavitary application for carcinoma of the cervix at the University of Alabama in Birmingham over a 10 year period from 1968 to 1981. There were 14 uterine perforations out of 799 intracavitary applications in 622 cases, an incidence of 1.77% of applications and 2.25% of cases. Ten cases were Stage I and 4 cases were Stage II. The high incidence of uterine perforation in Stage I was due to cervical scarring from previous conization of the cervix. Abortion of the application and careful monitoring is sufficient treatment in most cases. This view is supported by the uneventful post-perforation course in 12 of 14 cases. Of the 14 cases of uterine perforation, 9 (64%) underwent subsequent intracavitary application without further complication. Of these, 8 are still living or died without evidence of tumor. In the remaining 5 cases, it was impossible to locate the cervical canal on subsequent attempts. These underwent a variety of alternative treatments. Their therapeutic results and analysis of failures will be discussed. In this series, there is no direct evidence that uterine perforation alters the prognosis in radiation therapy of carcinoma of the cervix. (no Refs)

24. PROGNOSTIC AND TREATMENT FACTORS AFFECTING LOCAL CONTROL OF STAGE IB-IIA-B CARCINOMA OF THE INTACT UTERINE CERVIX TREATED WITH RADIATION THERAPY ALONE (MEETING ABSTRACT).

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Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

This is a retrospective analysis of 264 patients with stage IB - IIA-B carcinoma of the cervix treated with curative intent from October 1964 through April 1980. There is a minimum 2 year followup. Patients dead of disease with the pelvis controlled (13), dead from intercurrent disease (14), or lost to followup (1) at less than 24 months from treatment are excluded from analysis of local control. All patients are included in analysis of survival. Patient age, hematocrit, and tumor size were noted to be significant prognostic factors with regard to control of disease in the pelvis in stage IB and IIA cancers. Patient age and hematocrit were of particular prognostic value for patients with large lesions, greater than or equal to 6 cm in diameter. In contrast, only tumor size appeared to influence local control in stage IIB cancers. Overall treatment time appeared to influence local control in both stage IB - IIA-B disease when the size of the lesion was greater than or equal to 6 cm, as opposed to lesions less than or equal to 6 cm in diameter. In addition, the amount of tumor regression noted at the time of the radium application, after 4-5 weeks of external beam irradiation, appeared to be a predictor of local control in stage IIB lesions greater than or equal to 6 cm in diameter, whereas this did not hold true for stage IB-IIA lesions. The local control rate by stage and tumor size were IB less than or equal to 6 cm (91%), IB greater than or equal to 6 cm (73%), IIA (88%), IIB less than or equal to 6cm (85%), and IIB greater than or equal to 6 cm (66%). Five-year absolute and determinate survivals by stage and tumor size were IB less than or equal to 6 cm (71% and 87%), IB greater than or equal to 6 cm (68% and 82%), IIA (71% and 79%), IIB less than or equal to 6 cm (70% and 81%), and IIB greater than or equal to 6 cm (43% and 53%). (no Refs)

25. SELECTIVE CONTINUOUS CATHETERIZATION AND CYTOSTATIC INFUSION IN ADVANCED CARCINOMA OF THE CERVIX.

Falappa P, Cotroneo AR, Danza FM, Santini A, Trodella L, Turriziani A, Pastore G
Dept. Radiology, Universita Cattolica del S. Cuore, Roma, Italy
Excerpta Med Int Congr Ser; 575:161-164 1982

A crossed bilateral catheterization using the transfemoral approach was performed in 21 patients (10 Stage IIIB and 11 Stage IV) with carcinoma of the cervix. Arteriography was performed prior to and after infusion with adriamycin and methotrexate, both in doses of 10 mg/24 hr, diluted in 500 ml saline, and administered sequentially for 10-15 days until sys-

temic toxicity was observed. Regional infusion therapy induced complete response in six Stage IIIB and two Stage IV patients, partial response in three Stage IIIB and five Stage IV, and no response in one Stage IIIB and four Stage IV. The results were calculated from angiography, chemotherapy, and clinical control data. After intraarterial chemotherapy, all the patients underwent external radiotherapy, nine Stage IIIB and two Stage IV patients after-load curietherapy, and two Stage IIIB patients surgery. No important secondary effects justifying the interruption of therapy were observed. No arteritis or embolization occurred. Leukopenia and thrombocytopenia observed at the end of therapy were transient and did not affect the following treatment. Results indicated that selective intraarterial infusion chemotherapy should be considered as the first choice therapeutic approach in patients with advanced carcinoma of the cervix. (5 Refs)

26. CHEMOTHERAPEUTIC TREATMENT OF ENDOMETRIAL CARCINOMA.

Deppe G
Mount Sinai Hosp. Medical Center, Chicago, IL
Clin Obstet Gynecol; 25(1):93-99 1982

The available data on the use of hormonal and nonhormonal chemotherapy in the treatment of patients with endometrial cancer (EC) are summarized. Analysis of reports of treatment of advanced or recurrent EC with progestins showed an objective response with 17-alpha-hydroxyprogesterone caproate in 32% of patients. Discovery of steroid receptors might help to explain the therapeutic action of progestational agents in advanced EC. Hormonal effects are mediated by complexes formed by interaction of the steroid and its receptors. Tumors that lack receptors are unresponsive to the hormone. Thus, patients with EC devoid of progesterone receptors will not respond to progestin therapy. An objective response to tamoxifen of 30% was observed in 10 patients. The role of nonhormonal therapy in the management of EC has been restricted because of the previously demonstrated response of this tumor to surgery, radiotherapy, and progestins. Chemotherapy is employed most often for recurrent or advanced tumors beyond the control of surgery and irradiation. Single agents in treatment of EC are 5-fluorouracil (5-FU), cyclophosphamide (CY), adriamycin (ADM), and cis-platinum. Only two controlled prospective trials have evaluated the efficacy of combination chemotherapy regimens in patients with advanced and recurrent EC. One compared the efficacy of melphalan, 5-FU, and megestrol acetate (MEA) with CY, ADM, 5-FU, and MEA; and the other CY, ADM, and MEA with CY, 5-FU, and MEA. The overall objective response rate of combination chemotherapy regimens was not higher than the objective response rate for single-agent therapy with ADM. (40 Refs)

27. TREATMENT OF HYPERPLASIA AND CARCINOMA IN SITU OF THE ENDOMETRIUM.

Kistner RW
Harvard Medical Sch., Boston, MA
Clin Obstet Gynecol; 25(1):63-74 1982

Therapy for hyperplasia and carcinoma in situ of the endometrium in patients of different ages is reported. The endocrine role of initiation and progression of endometrial cancer and endometrial hyperplasia and carcinoma of the endometrium are reviewed. Rationale for endocrine therapy is discussed. Case reports are presented illustrating the management of endometrial hyperplasia and carcinoma in situ in patients who desire children, in patients prior to hysterectomy, and in inoperable patients. Postpubescent patients with endometrial hyperplasia and carcinoma in situ should receive estrogen-progestin in artificial cycles for 6 mo and ovulation should be secured. Patients of child-bearing age should have ovulation secured with the use of cortisone, clomiphene, or wedge resection of the ovaries or estrogen-progestin, or progestin alone in artificial cycles for 6-12 mo. Premenopausal patients should have progestin artificial cycles until the age of 50-52 yr; hysterectomy should be performed in uncontrollable cases. Postmenopausal women should undergo hysterectomy; if inoperable, constant im progestin should be administered for 1 yr. Approx 10% of patients with atypical endometrial hyperplasia will eventually develop invasive carcinoma if untreated. Cells in glands that subsequently become cancerous exhibit abnormal DNA distribution and aneuploidy. (24 Refs)

28. TREATMENT RESULTS IN CARCINOMA OF THE CERVIX STAGE IB IN A TOTAL POPULATION.

Iversen T, Kjorstad KE, Martimbeau PW
Dept. Gynecology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Gynecol Oncol; 14(1):1-5 1982

A total of 709 patients with Stage IB squamous cell carcinoma of the cervix were treated 1967/1972. In 20 cases primary surgery with radical hysterectomy and pelvic lymphadenectomy was performed, 542 received preoperative intracavitary radium treatment, and 147 received intracavitary and external irradiation. The 5-yr survival rate for the operated patients was 86% as compared to 82% for the 131 who received a full course of radiotherapy. The distribution of recurrences and the frequency of fistulas was the same in these two groups. (Author abstract) (8 Refs)

29. ENDOMETRIAL CARCINOMA: STAGE I. A RETROSPECTIVE ANALYSIS OF 262 PATIENTS.

De Palo G, Kenda R, Andreola S, Luciani L, Musumeci R, Rilke F
Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy
Obstet Gynecol; 60(2):225-231 1982

From 1969 to 1977, 420 patients with endometrial carcinoma were observed and treated at the National Tumor Institute of Milan. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed in 351. After careful clinical and pathologic review, 262 patients were classified as having Stage I disease. Further treatment included postoperative radium therapy to the vaginal vault. There were 247 cases with adenocarcinoma, 10 with adenoacanthoma, and 5 with adenosquamous or clear cell carcinoma. Of 257 cases with adenocarcinoma or adenoacanthoma, 63 were Grade 1, 161 Grade 2, and 33 Grade 3. Of the total series, only 41 cases had disease limited to the mucosal surface. The 5-yr actuarial survival was 91.4% and the recurrence-free survival was 93.4%. The case material was evaluated according to the risk factors, and results were (1) premenopausal patients had a better prognosis (100% recurrence-free survival vs 92.8% for postmenopausal women, $p = .003$); (2) length of the uterine cavity was not a significant prognostic factor; (3) myometrial invasion alone was not prognostic but correlated with grade of tumor; (4) the grade of the tumor was an important determinant of recurrence (Grade 1 98% recurrence-free survival, Grade 2 95%, Grade 3 79%). With the described therapy, vaginal recurrences were absent. The recurrences were distant in 20% and local with or without distant metastases in 80%. (Author abstract) (26 Refs)

30. STAGE IB CARCINOMA OF THE CERVIX, THE NORWEGIAN RADIUM HOSPITAL. II. RESULTS WHEN PELVIC NODES ARE INVOLVED.

Martimbeau PW, Kjorstad KE, Iversen T
Gynecologic Oncology, 1900 Randolph Road, Suite 510, Charlotte, NC, 28207
Obstet Gynecol; 60(2):215-218 1982

From 1967 through 1972, 562 patients with squamous cell carcinoma of the cervix, Stage IB (FIGO), underwent radical hysterectomy with pelvic lymphadenectomy. The patients with pelvic metastases were treated with external beam supervoltage irradiation of 4,000 or 5,000 rads to the pelvis. Metastases in the pelvic lymph nodes were found in 21.3%. In this study the authors analyzed in detail which nodes were involved with metastases and the relationship with survival and with recurrence. The overall 5-yr survival for patients with pelvic lymph node metastases was 53%; for patients without metastases it was 92%. The site of recurrence in patients without demonstrable pelvic lymph node metastases was also examined. The main conclusion drawn from the study is that patients with pelvic node metastases below the common iliac group have a much better prognosis than patients in whom metastases are located in the common iliac nodes; in addition, when nodal involvement is below the common iliac level, patients with disease limited to one node or one group of nodes do not have a better prognosis than patients with multiple metastatic nodes. (Author abstract) (10 Refs)

31. OBSERVATIONS ON THE DEVELOPMENT OF DYSPLASIA.

Heinzl S, Szalmay G, Jochum L, Roemer V
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Acta Cytol (Baltimore); 26(4):453-456 1982

In order to more effectively monitor women with dysplasia of the uterine cervix, a dysplasia clinic was established at the University Women's Hospital, Basel, in 1970. From 1970 to 1978, 3,570 women were examined in the clinic. The mean age of the patients was 36.4 +-13.3 years. Since in most cases we administer therapy to women whose cervical smear reports indicate at least severe dysplasia, we devoted our attention to those patients with smears showing mild-to-moderate dysplasia. Of the 2,528 women who had such smears, 111 were not followed up in our clinic. Mild-to-moderate dysplasia was demonstrated only once in 1,110 patients and was found at least twice in 1,051 women. Progression to a cervical smear showing at least severe dysplasia occurred in 256 patients (10%). This progression, however, was demonstrated in 87% of the 256 patients as early as the first 2 years of monitoring. Our observations make it clear that strict surveillance of patients with dysplasia even in the mild or moderate stage is necessary. With strict monitoring, the anticipated progression in 10% of the patients can be detected early; as a result, we can achieve successful secondary prophylaxis of cervical carcinoma. (Author abstract) (11 Refs)

32. A COHORT STUDY OF CERVICAL CANCER SCREENING IN BRITISH COLUMBIA.

Boyes DA, Morrison B, Knox EG, Draper GJ, Miller AB
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Clin Invest Med; 5(1):1-25 1982

A cohort study was conducted using the records of the British Columbia Screening Program for the years 1949-69. Records were extracted for two cohorts of women: 52,452 born between 1914-18 and 66,701 born between 1929-33. Corrections were applied for duplication, deaths from all causes, hysterectomies, in- and out-migration, and the women-years under surveillance (defined as the period from the first to the last observed smear) were calculated. Corrections were also applied for observed and not observed false-negative findings on initial and subsequent examination. Estimation of error rates of screening and diagnostic procedures and refinement of the understanding of the natural history of cervical cancer were attempted. Numerous sources of error in the data and methods of their correction are discussed. Regression appears to be an important part of the natural history of both dysplasia and carcinoma in situ. Dysplasia was diagnosed more frequently at later ages in both cohorts and seemed to behave as a manifestation of pre-clinical cancer which infrequently progresses to clinical disease. Carcinoma in situ seemed to achieve maximal incidence rates relatively early in life, with a peak at ages 30-34 yr in the present study, and decreased fairly rapidly thereafter. Regression of carcinoma in situ seemed to occur more frequently at younger ages. The probability of progression of carcinoma in situ to the invasive state is greater at older ages. (16 Refs)

33. DEFINITION OF ENDOMETRIAL CARCINOMA PRECURSORS.

Scully RE
Massachusetts General Hosp., Boston, MA
Clin Obstet Gynecol; 25(1):39-48 1982

Current knowledge of precancerous lesions of the endometrium is reviewed. Precancerous lesions are generally classified as either cystic hyperplasia or complex hyperplasia. While no national or international classification system is available, precancerous lesions of the endometrium exhibit cystic hyperplasia, atypical (proliferative) hyperplasia, atypical secretory hyperplasia, carcinoma in situ, polyp, or a mixture of the aforementioned changes. Great variations in classification and definition of terms in the literature make formulations of conclusions or a therapeutic program difficult. Each classification is described in detail. Endometrial metaplasia can be squamous, papillary syncytial, ciliated cell, eosinophilic, mucinous, hobnail cell, or clear cell. Some endometrial changes may be misinterpreted as precancerous. Features necessary for a diagnosis of adenocarcinoma include epithelial stratification with loss of radial orientation of cells, glandular architecture complexity with budded and branched glands and cribriform pattern, luminal polymorphs and necrosis, and cytologic atypia with large cells, high nuclear-cytoplasmic ratio, nuclear pleomorphism, prominent nucleoli, abnormal chromatin configuration, angulated nuclear membranes, and mitotic figures. Estrogens and precancerous lesions and endometrial polyps are discussed. Cellular atypicality is of greater importance than architectural abnormalities in risk of development of carcinoma. The most serious precancerous lesion is probably the combination of severe cytologic and architectural atypicality. An internationally acceptable classification of precancerous lesions of the endometrium is needed. (23 Refs)

OVARIAN AND FALLOPIAN TUBE TUMORS

34. GYNANDROBLASTOMA. ITS ULTRASTRUCTURE.

Chalvardjian A, Derzko C
Dept. Pathology, St. Michael's Hosp., 30 Bond St., Toronto, Ontario M5B 1W8, Canada
Cancer; 50(4):710-721 1982

Gynandroblastoma is a rare, sex-cord stromal tumor of the ovary that shows morphologic evidence of female and male differentiation. Such a tumor produced masculinization in a 24-yr-old woman, whose symptoms disappeared following removal of the tumor. By electron microscopy, the granulosa cell nests displayed Call-Exner (CE) bodies of the hyaline type composed of multiple layers of basal lamina resembling CE bodies of the normal graafian follicle. In contrast, CE bodies of a classic granulosa theca cell tumor were of the spongiform type, consisting of a space limited by a single basal lamina containing altered granulosa cells and cell processes. Both types of CE bodies are believed to arise following secretion by and/or degeneration of granulosa cells, the variation in morphology between the two resulting from differences in amounts of basal lamina deposited. The tubular components of the tumor resembled more closely the rete ovarii than they did Sertoli cells, and it is proposed that such structures be called by the alternate and less specific term 'androblastoma'. The identity of Leydig cells was established by demonstration of intracytoplasmic Reinke crystals. Despite a difference in architectural pattern, there was a close ultrastructural resemblance between the different sex-cord components of the gynandroblastoma. (Author abstract) (35 Refs)

35. PROGNOSTIC IMPORTANCE OF PSAMMOMA BODIES IN ADENOCARCINOMAS OF THE OVARIES.

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Gynecol Oncol; 14(1):6-14 1982

Microcalcifications called psammoma bodies are a common finding in serous papillary adenocarcinomas of the ovary. In a series comprising 501 cases of ovarian carcinoma the prognostic importance of the presence of these calcifications is analyzed. Psammoma bodies are confined mainly to serous papillary adenocarcinomas, particularly stage III. Using a life-table technique for survival analysis, it was not possible to demonstrate a significant difference in survival rates in cases with and without such calcifications, although the histological type, tumor stage, and grade, all known to be of prognostic importance, are kept constant. Supportive evidence favors the theory that psammoma body formation is a consequence of dystrophic calcification associated with ischemia rather than tumor-host hypersensitivity-related cell death. (Author abstract) (9 Refs)

36. RADIOTHERAPY IN EPITHELIAL OVARIAN CANCER: 24 YEARS' EXPERIENCE - PRETREATMENT PROGNOSTIC FACTORS (MEETING ABSTRACT).

Schray M, Cox R, Martinez A
Stanford University Medical Center, Stanford, CA
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Between 1956 and 1980, 152 patients with FIGO stages I, II and III epithelial carcinoma of the ovary were treated with lower abdominal or whole abdominal/pelvic megavoltage radiotherapy techniques as sole postoperative treatment. The prognostic factors of stage, amount of postoperative residual disease, histologic type, grade and age were retrospectively analyzed. All freedom from relapse (FFR) values are quoted at 10 years and mean follow-up was 6.0 years. For the entire group, FFR was 45%. FFR for stages I, II and III was 81%, 60% and 13% respectively. For patients with no residual disease, FFR was 72%; for those with minimal residual disease of less than 2 cm, 50%; and for those with gross residual disease of greater than 2 cm, 17%. Histologic grade was termed well, moderately, or poorly differentiated with FFR of 86%, 70% and 21% respectively. The most frequently seen histologic subtypes were endometrioid, serous and undifferentiated with their FFR being 65%, 45% and 7% respectively. In patients younger that 40 years of age, the FFR was 80% as compared to 38% for those 40 years and older. Multivariate analysis showed all factors to have individual prognostic significance with histologic grade of greatest significance with $p = 0.005$; age, $p = 0.004$; residual disease, $p = 0.007$; stage, $p = 0.015$; and histologic type, $p = 0.025$. Prognostic profile based on the simultaneous correlation of grade, residual disease and stage define those having a good, intermediate or poor prognosis utilizing postoperative radiotherapy alone. This provides a basis for recommending whole abdominal/pelvic irradiation for specific groups and defining those patients who require other therapy. (no Refs)

37. TREATMENT OF RECURRENT AND PERSISTENT GERM CELL TUMORS WITH CISPLATIN, VINBLASTINE, AND BLEOMYCIN.

Jacobs AJ, Harris M, Deppe G, DasGupta I, Cohen CJ
Dept. Obstetrics and Gynecology, Univ. Nebraska Medical Center, Omaha, NE, 68105
Obstet Gynecol; 59(1):129-132 1982

Four patients were treated with vinblastine, cisplatin, and bleomycin for recurrent or persistent germ cell tumors. In all patients a clinical response was achieved. In two patients complete response was attained and they are free of disease following second-look laparotomy. One had a mixed germ cell tumor that persisted as dysgerminoma following primary chemotherapy. The other was a true hermaphrodite with pure dysgerminoma. In patients with endodermal sinus tumor transient response was achieved, but the tumors recurred and the patients died within 6 mo. (Author abstract) (16 Refs)

38. POTENTIAL FOR CURE IN METASTATIC OVARIAN TERATOMAS AND DYSGERMINOMAS.

Newlands ES, Begent RH, Rustin GJ, Bagshawe KD
Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England
Br J Obstet Gynaecol; 89(7):555-560 1982

Treatment results are reported for 21 patients (5-41 yr old; mean 19.3 yr), 18 with malignant ovarian teratomas (MOT) and 3 with dysgerminomas (DYS). Sequential chemotherapy was administered according to the following combinations: Treatment A, vincristine, methotrexate, bleomycin, folinic acid rescue, forced diuresis and hydration, and cis-platinum; Treatment B, VP-16213, actinomycin D, and cyclophosphamide; Treatment C, hydroxyurea, vinblastine, and chlorambucil; and Treatment D, the same as Treatment A, but without hydration and cis-platinum. Among 14 MOT who survived, 13 had no treatment for 1-45 mo (mean 27.5 mo); 12 of these were in complete clinical and biochemical remission. One patient had a partial response and only one patient failed to respond and died. The other patients who died did so before adequate chemotherapy could be given, had a partial response but the

tumor became resistant, or initially responded well to cytotoxic chemotherapy but experienced massive abdominal recurrence. The mean duration of treatment in the 13 patients who completed chemotherapy was 6.8 mo. Toxicity included leukopenia, thrombocytopenia, and transient rises in serum creatinine concentrations. All patients experienced transient alopecia. The three patients with DYS had extensive abdominal disease: two of these patients achieved complete remission on chemotherapy alone, one required surgery. Most metastatic germ cell tumors of the ovary are curable if treated early enough with chemotherapy. (19 Refs)

39. PROGESTOGEN THERAPY FOR OVARIAN CARCINOMA.

Timothy I
Dept. Obstetrics and Gynaecology, Leighton Hosp., Crewe, Cheshire, England
Br J Obstet Gynaecol; 89(7):561-563 1982

Treatment of 15 women (31-75 yr old) with ovarian carcinoma with a new progestogen, gestronol hexanoate (GHX), is reported. Most patients received one injection of 200 mg GHX/wk; when tumor size increased or when the patient felt unwell, the dose was increased to 400 mg 1x/wk or 200 mg 2x/wk. While duration of survival was not increased, the quality of life was improved by a sense of well-being despite advanced disease. Many of the patients remained well, gained wt, and had no sign of recurrence for periods up to 72 mo. GHX was administered immediately after surgery or up to 1 wk after diagnosis. Most of these patients had been treated previously with alkylating agents after surgery; however, side effects outweighed the improvements noticed. Nine of the patients were alive with no recurrence of growth for 6-72 mo from the first dose of GHX. Five patients experienced recurrence 9-24 mo after the first GHX dose. One patient exhibited a decrease in tumor size allowing easy excision. Use of GHX is recommended for improving the quality of life of patients with ovarian carcinoma. (3 Refs)

40. GASTRIC OUTLET OBSTRUCTION CAUSED BY ASCITIC FLUID ENTRAPMENT IN THE LESSER SAC - A COMPLICATION OF ADVANCED OVARIAN CANCER: REPORT OF TWO CASES.

Krebs HB, Walsh J, Goplerud DR
Dept. Obstetrics and Gynecology, Medical Coll. Virginia, Richmond, VA. 23298
Gynecol Oncol; 14(1):105-111 1982

Two patients are reported with advanced ovarian cancer presenting with symptoms suggesting gastric outlet obstruction. In each case the symptomatology and clinical findings were caused by gastric compression secondary to entrapment of ascitic fluid in the lesser sac. This complication may be suggested by an upper gastrointestinal series, but is unequivocally diagnosed by computed tomography. Resection of the lesser omentum, repeat paracenteses, or insertion of a LeVeen peritoneovenous shunt into the lesser sac may all be used therapeutically for decompression of the stomach. (Author abstract) (2 Refs)

TROPHOBLASTIC DISEASE

41. SURGERY IN METASTATIC TROPHOBLASTIC DISEASE.

Ratnam SS, Llancheran A
Dept. Obstetrics and Gynecology, Natl. Univ. Singapore, Kandang Kerbau Hosp., Singapore, Singapore
Semin Oncol; 9(2):221-223 1982

The role of surgery in metastatic trophoblastic disease may be limited to complications involving gastrointestinal or urinary tract obstruction, relief of increasing intracranial pressure, control of not manageable hemorrhage, removal of drug-resistant disease, and the removal by craniotomy of certain brain secondaries. Pulmonary metastases occur up to 70% of the cases of gestational choriocarcinoma. Resection of a solitary pulmonary lesion without preliminary treatment with chemotherapy has a two-fold risk. First, the presence of other foci of choriocarcinoma undetected radiologically may cause anxiety after thoracotomy. Second, the operative procedure itself may disseminate the growth to other parts of the body and to the brain in particular. In the event of resistance to chemotherapy, the early resection of the pulmonary nodule is imperative. Cerebral metastases are reported in 10-20% of patients with choriocarcinoma. A review of methods of management of cerebral metastases shows that total brain irradiation (3,000-4,000 rads) with combined chemotherapy gives the best results. The appearance of vaginal nodules occurs in about 1.3% of the cases of gestational trophoblastic disease. Chemotherapy is very effective in causing rapid regression of the lesions. Excision should not be attempted in patients who are bleeding because such nodules are extremely hemorrhagic. (10 Refs)

42. THE ROLE OF SURGERY IN THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC DISEASE.

Clayton LA, Barnard DE, Weed JC, Hammond CB
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Semin Oncol; 9(2):213-220 1982

The current status of surgical intervention in the comprehensive care of patients with gestational trophoblastic neoplasia (GTN) is reviewed. Common indications for surgical intervention in GTN are: control of bleeding, relief of urinary or bowel obstruction, resection of residual, resistant disease, or the adjunctive treatment of infection. Hysterectomy coincident with the institution of systemic chemotherapy can significantly reduce the duration of hospitalization and the amount of chemotherapy needed to achieve remission, regardless of whether or not metastases are present. Delayed surgical excision of chemotherapy-resistant foci is less effective than as an initial surgery. Clinical problems in patients with GTN, possible indications for surgery, the use of pelvic arteriography to localize GTN, surgery and benign trophoblastic disease, surgery and nonmetastatic trophoblastic disease, surgery for patients with metastatic GTN with good prognosis, surgery in metastatic poor prognosis GTN, the role of thoracotomy, and excision of other resistant metastatic foci are also discussed. (32 Refs)

43. NEW CHEMOTHERAPEUTIC AGENTS IN THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC DISEASE.

Newlands ES
Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England
Semin Oncol; 9(2):239-243 1982

Techniques of systemic chemotherapy used against gestational trophoblastic neoplasia at Charing Cross Hospital are discussed. In patients becoming resistant to methotrexate (MTX), the only active agents were found to be actinomycin-D and 6-azauridine. A combined response and improvement rate of 62% was observed in 24 drug-resistant patients treated with vincristine (VCR), MTX, and cis-platinum. All of these patients had previously extensive therapy using VCR and MTX in the multidrug CHAMOMA regimen. Some patients who have received the protocol containing cis-platinum have now been off treatment and in complete remission for up to 37 mo. In view of the side effects from cis-platinum, however, this treatment is limited to those who have become resistant to all other cytotoxic therapy. VP 16-213, a well tolerated drug with clear-cut activity in drug-resistant disease, has been successfully used as an initial chemotherapy, followed by a cycling sequence of drug therapy. Twenty-three of 23 patients resistant to other drugs have experienced reduction in human chorionic gonadotropin levels following VP 16-213. The integration of VP 16-213 and possibly also cis-platinum early in chemotherapy for selected patients may contribute to the cure of some cases who would otherwise become drug resistant. (16 Refs)

44. THE MANAGEMENT OF POOR PROGNOSIS TROPHOBLASTIC DISEASE.

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Southwestern Regional Trophoblastic Disease Center, Univ. Arizona Health Sciences Center, Tucson, AZ, 85724
Semin Oncol; 9(2):204-207 1982

Advances in the treatment of gestational trophoblastic neoplasia have occurred due to the inherent sensitivity of these tumors to chemotherapy, the use of human chorionic gonadotropin as a tumor marker, and the identification of high-risk factors which allow a greater degree of individualization of therapy. CNS metastases, liver metastases, frequency of therapy, alternative treatment modalities in resistant disease, reelevation of HCG titers due to isolated tumor foci, and adjuvant hysterectomy or resection of metastases are also discussed. (12 Refs)

45. CHORIOCARCINOMA METASTATIC TO THE BRAIN: THERAPY AND PROGNOSIS.

Weed JC, Woodward KT, Hammond CB
Gynecology/Oncology, Univ. South Alabama Coll. Medicine, 2451 Fillingim St., Mobile, AL, 36617
Semin Oncol; 9(2):208-212 1982

The experience of the Southeastern Regional Trophoblastic Disease Center in the Therapy of 23 patients suffering cerebral metastases of gestational trophoblastic neoplasia is reported. Cerebral metastases are found in 14-18% of patients with disseminated gestational trophoblastic neoplasia. All of the patients in the present series had pulmonary metastatic disease in addition to cerebral metastases. Symptoms of CNS disease were present in 18/23 patients. Four patients were found to have silent brain lesions when restaged for failure to respond to therapy, and necropsy revealed an unsuspected brain lesion in one patient. Seven of 11 patients who presented initially with evidence of brain lesions were treated successfully. Only two of nine patients survived who developed brain lesions while undergoing systemic chemotherapy. Three patients in remission returned with recurrent disease and CNS metastases. Only one of these three survived. Specific therapeutic regimens for cerebral metastases are described. Nineteen patients received whole brain irradiation in addition to multiple-agent chemotherapy. The 10 surviving patients received whole brain 60Co irradiation in doses ranging from 2,000-3,300 rads coincident with the onset of chemotherapy. (8 Refs)

46. NONMETASTATIC AND LOW-RISK METASTATIC GESTATIONAL TROPHOBLASTIC NEOPLASMS.

Goldstein DP, Berkowitz RS
New England Trophoblastic Disease Center, Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
Semin Oncol; 9(2):191-197 1982

Management of nonmetastatic and low-risk metastatic gestational trophoblastic neoplasia (GTN) is discussed. About 15% of patients develop nonmetastatic GTN following molar removal. Hemorrhage due to trophoblastic uterine perforation is a serious complication. Single agent chemotherapy is the treatment of choice, and methotrexate (MTX) and citrovorum factor (CF) is the preferred regimen. If a patient with nonmetastatic GTN no longer wishes to preserve fertility, hysterectomy plus adjuvant chemotherapy may be recommended. patients with nonmetastatic GTN are advised not to become pregnant until 12 mo of normal human chorionic gonadotropin levels have been achieved. Trophoblastic tumors metastasize in about 5% of patients following molar removal and infrequently after other gestational events. Sequential single agent chemotherapy with MTX-CF and actinomycin D has induced complete remission in 79/95 patients with low risk metastatic GTN. The remaining 16 patients achieved complete remission with combination chemotherapy with or without local resection. Protocols for the management of resistant disease are described. Surgical therapy plays a limited role in the management of low-risk metastatic GTN. (17 Refs)

47. THE MANAGEMENT OF HIGH-RISK CHORIOCARCINOMA.

Begent RH, Bagshawe KD
Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England
Semin Oncol; 9(2):193-203 1982

Intensive treatment methods developed for 72 high-risk patients with invasive mole and choriocarcinoma are described. The major factors that influence prognosis are tumor burden as reflected in human chorionic gonadotropin values, the interval between antecedent pregnancy and time of diagnosis, the presence of large metastases, metastases in brain, liver or kidney, and the ABO group of the patient and her husband. The immediate risk associated with choriocarcinoma is usually related to metastases that are present in the great majority of high-risk patients at presentation. Large masses of choriocarcinoma, whether in the uterus, liver, lungs, or brain, are usually enmeshed in a network of large and delicate vessels so that surgery may be hazardous in the extreme. Radiotherapy to a brain metastasis at the outset of treatment may, like chemotherapy, precipitate a rise in intracranial pressure due to physical changes around the tumor. While chemotherapy is the treatment of choice, physical changes sometimes occur within or around the tumor leading to an initial increase in size. In this series, 6/72 patients have died as a result of the initial extent of disease. Most patients do not have immediate life-threatening

disease at the time of diagnosis. Principles of management, drug resistance, surgery and radiotherapy for drug resistant disease, and treatment of central nervous system metastases are also discussed. (8 Refs)

48. HYDATIDIFORM MOLE AND GESTATIONAL TROPHOBLASTIC DISEASE IN SOUTHERN CONNECTICUT.

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Obstet Gynecol; 59(1):78-84 1982

Of 127 patients with hydatidiform mole in southern Connecticut, 34 (28%) received chemotherapy for persistently elevated human chorionic gonadotropin (hCG) titers. An hCG regression curve was found to be useful if not mandatory for following patients. Excess uterine size, theca lutein cysts, uterine bleeding, and histologic trophoblastic hyperplasia were relative discriminators of the need for chemotherapy. In the absence of metastases, an hCG titer was the only valid discriminator for initiating chemotherapy, provided the patient could be followed consistently and reliably. The indications for initiating chemotherapy are discussed. Early diagnosis and close follow-up were associated with low morbidity. Five of six patients with metastatic disease were referred from outside the center. (Author abstract) (23 Refs)

49. UTERINE CHORIOCARCINOMA WITH NEGATIVE SPECIFIC SERUM RADIOIMMUNOASSAY FOR HUMAN CHORIONIC GONADOTROPINS.

Bakri Y, Lee JH, Jahshan AE, Lewis GC
Dept. Obstetrics and Gynecology, Eastern Virginia Medical Sch., 603 Medical Tower, Norfolk, VA, 23507
Gynecol Oncol; 14(1):112-118 1982

A case of uterine choriocarcinoma complicating gestational trophoblastic disease is presented. Following chemotherapy, there seemed to be an apparent cure as indicated by follow-up monitoring of the beta subunit of human chorionic gonadotropin (B-HCG assay) when the assay demonstrated three consecutive weekly negative results. At the same period when the assays were negative, the patient was manifesting irregular vaginal bleeding for which diagnostic D and C was done revealing persistent disease which was not detected by measurement with the sensitive quantitative B-HCG assay. The case is discussed to confirm the fact that clinical assessment is necessary for the follow-up of trophoblastic disease in addition to quantitative B-HCG. (Author abstract) (2 Refs)

MULTI-SITE STUDIES AND REVIEWS

50. PALLIATIVE EMBOLISATION IN GYNAECOLOGIC MALIGNANCIES.

Schuur KH, Bouma J
Dept. Diagnostic Radiology, Univ. Hosp., Groningen, The Netherlands
Excerpta Med Int Congr Ser; 575:120-124 1982

Effects of palliative embolization were studied in eight patients (42-89 yr old) with gynecologic malignancies. All patients had chronic loss of blood and anemia. The percutaneous catheterization was applied. Gelfoam particles (2 patients), Gianturco-coils (4), and combination of both techniques (2) were used. Survival of the patients ranged from 10 days to 8 mo. Three patients were still alive. One patients died 10 days after embolization. The patient had signs of necrosis in the minor pelvis prior to embolization. Obduction showed the necrosis and extent of abscesses. One patient got an anus praeternaturalis because of ileus. In three of the five patients who died, embolization had a good effect on anemia. A temporarily dull feeling and some pain in the upper leg and buttocks were observed in some patients in whom embolization was performed ahead of the gluteal branches. In most of the patients the temperature was subfebrile for several days. Inflammation and abscess formation could be a serious complication in patients with ulcerating tumors. Therefore, antibiotics, flagyl and cephuroxin, or flagyl and tobramycin should be administered prior to the procedure, provided that the renal function is no contraindication. (7 Refs)

51. ISOLATION OF A HUMAN PAPILLOMAVIRUS FROM A PATIENT WITH EPIDERMODYSPLASIA VERRUCIFORMIS: PRESENCE OF RELATED VIRAL DNA GENOMES IN HUMAN UROGENITAL TUMORS.

Green M, Brackmann KH, Sanders PR, Loewenstein PM, Freel JH, Eisinger M, Switlyk SA
Inst. Molecular Virology, St. Louis Univ. Medical Center, St. Louis, MO, 63110
Proc Natl Acad Sci USA; 79(14,part1):4437-4441 1982

The DNA genome of a human papillomavirus (HPV), tentatively designated HPV-EV, was molecularly cloned from hand and leg lesions of a patient with epidermodysplasia verruciformis, a chronic skin disease associated with a 30% risk of developing cancer. Using stringent hybridization conditions, we observed less than 5% homology between HPV-EV and the cloned genomes of HPV-1, HPV-4, HPV-5, and HPV-5a. HPV-EV DNA showed approx 6% homology with HPV-2 and 36% homology with HPV-3. These data suggest that HPV-EV is partially related to HPV-3. Using 32P-labeled cloned HPV-EV as probe in Southern blot hybridization experiments, we detected HPV-EV-related DNA in the carcinoma in situ (Bowenoid lesion) of the vulva of the patient from which HPV-EV was isolated. HPV-EV-related DNA was detected in 2 of 10 vulva carcinomas and in 2 of 31 cervical carcinomas. Related DNA sequences were found in papillomas from each of two patients with condyloma acuminata (anogenital warts), which is of interest considering that condylomas have been reported to convert occasionally to carcinomas. The positive vulva DNAs were also probed with other cloned HPV DNAs: HPV-1-, HPV-4-, and HPV-5a-related sequences were not detected: HPV-3 and HPV-2 DNA probes detected strong and weak DNA bands, respectively, of the same size as found with HPV-EV. The HPV DNA sequences were present in the positive tumors mainly as free viral DNA moleculars: no evidence for integration into cellular DNA was found. The emerging biological picture with papillomaviruses is that cells transformed by these viruses are maintained in a transformed state by free episomal genomes. Thus, our findings are consistent with the idea, but by no means establish, that HPVs play a role in human cancer by a similar mechanism. (Author abstract) (24 Refs)

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